TRANSACTIONS

OF THE

AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS

VOLUME XXXIV

TRANSACTIONS

OF THE

AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS

Fifty-third Annual Meeting held at
Hot Springs, Virginia

May 29, 30 and 31, 1941

Volume XXXIV

Published for the Association by
The Bruce Publishing Company
Saint Paul and Minneapolis
1941

UNIVERSITY OF
MINNESOTA
LIBRARY

JUL 7 '47 U OF M BINDERY

OFFICERS OF THE ASSOCIATION FOR 1940-1941

President

MONTAGUE BOYD, M.D., Atlanta

Vice President

HOMER G. HAMER, M.D., Indianapolis

Secretary-Treasurer

CHARLES C. HIGGINS, M.D., Cleveland
2020 East 93rd Street

Members of the Council

J. BAYARD CLARK, M.D., New York

J. A. C. COLSTON, M.D., Baltimore

THE PRESIDENT
THE VICE PRESIDENT
THE SECRETARY
} *Ex-Officio*

JUL 7 '47 U OF M BINDERY

1168388

LIST OF MEMBERS

HONORARY MEMBERS

Dr. Gardner W. Allen (1893), 146 Massachusetts Ave., Boston.
Dr. Charles H. Chetwood (1900), 25 Park Avenue, New York.
Dr. Charles L. Gibson (1901), The Burke Foundation, White Plains, N. Y.
Dr. Francis S. Watson (1888), South Dartmouth, Mass.
*Dr. William N. Wishard (1889), 1711 N. Capitol Ave., Indianapolis.
(4)

CORRESPONDING MEMBERS

Mr. E. Hurry Fenwick, C.B.E., F.R.C.S. (1906), 53 Bedford Gardens, Campden Hill, London, W. 8.
Prof. Emile Jeanbrau (1911). 1 Rue Barthez, Montpelier, France.
Mr. J. Swift Joly, M.D., F.R.C.S. (1934), 80 Harley Street, London, W. 1.
Prof. Dr. Med. A. von Lichtenberg (1929), Sanatorium Siesta, Budapest, Hungary.
Mr. John Pardoe, M.B., C.M., F.R.C.S. (1909), 1 Red House, Port Erroll, Aberdeen, Scotland.
Prof. Alfred Pousson (1909), 10 Cours Tournon, Bordeaux, France.
Prof. Jean René Verhoegen (1911), 98 Rue Marie Thérèse, Brussels, Belgium.
Prof. Dr. Med. Hans Wildbolz (1929), 12 Finkenhubelweg, Berne, Switzerland.
(8)

FELLOWS

Dr. Nathaniel G. Alcock (1922), University Hospital, Iowa City, Ia.
Dr. J. Dellinger Barney (1912), 374 Marlborough Street, Boston.
Dr. Benjamin S. Barringer (1911), 114 East 54th Street, New York.
Dr. William F. Braasch (1913), Mayo Clinic, Rochester, Minn.
Dr. Robert C. Bryan (1915), 2312 Monument Ave., Richmond, Va.
Dr. C. E. Burford (1926), 958 Arcade Building, St. Louis.
Dr. Hugh Cabot (1907), 465 Warren Street, Needham, Mass.
Dr. J. Bayard Clark (1906), 140 East 54th Street, New York.
Dr. Arthur H. Crosbie (1916), 520 Commonwealth Avenue, Boston.
Dr. John H. Cunningham (1906), 46 Gloucester Street, Boston.
Dr. H. A. Fowler (1907), 611-A Stoneleigh Court, Washington, D. C.
Dr. H. G. Fuller (1920), 209 Columbia Medical Bldg., Washington, D. C.
*Dr. Francis R. Hagner (1906), 209 Columbia Medical Bldg., Washington, D. C.
Dr. Homer G. Hamer (1923), 1711 N. Capitol Avenue, Indianapolis.
Dr. Frank Hinman (1920), 384 Post Street, San Francisco.
Dr. T. Leon Howard (1936), 1224 Republic Building, Denver.
Dr. Edward L. Keyes (1901), 121 East 60th Street, New York.
Dr. Herman L. Kretschmer (1916), 122 South Michigan Blvd., Chicago.

*Deceased.

Dr. Thomas F. Laurie (1922), 713 E. Genesee Street, Syracuse.
Dr. Bransford Lewis (1892), 609 Humboldt Building, St. Louis.
Dr. George R. Livermore (1922), 815 Medical Arts Building, Memphis.
Dr. William E. Lower (1912), 2020 East 93rd Street, Cleveland.
Dr. E. J. McCague (1934), Mercy Hospital, Pittsburgh.
Dr. J. F. McCarthy (1924), 2 East 54th Street, New York.
Dr. Charles M. McKenna (1926), 25 East Washington Street, Chicago.
Dr. Gordon F. McKim (1935), Union Central Bldg., Cincinnati.
Dr. David W. MacKenzie (1920), 1538 Sherbrooke St., W., Montreal.
Dr. Clarence R. O'Crowley (1935), 31 Lincoln Park, Newark, N. J.
Dr. Richard F. O'Neil (1909), 379 Beacon Street, Boston.
Dr. Alfred T. Osgood (1906), 65 E. 66th Street, New York.
Dr. Frank S. Patch (1923), 1225 Bishop Street, Montreal, Canada.
Dr. James Pedersen (1905), 55 Park Avenue, New York.
Dr. William C. Quinby (1916), 101 Bay State Road, Boston.
Dr. Nathaniel P. Rathbun (1921), 80 Hanson Place, Brooklyn, N. Y.
Dr. Louis E. Schmidt (1903), 709 Monroe Bldg., Chicago.
Dr. J. Bentley Squier (1906), 8 East 68th Street, New York.
Dr. Alexander R. Stevens (1916), 65 East 66th Street, New York.
Dr. William E. Stevens (1930), 490 Post Street, San Francisco.
Dr. Wm. P. Willard (1937), 450 Sutter Street, San Francisco.
Dr. Alfred C. Wood (1900), 2035 Walnut Street, Philadelphia.
Dr. Hugh H. Young (1901), Johns Hopkins Hospital, Baltimore.
(41)

ACTIVE MEMBERS

Dr. Wm. J. Baker (1940), 7 West Madison St., Chicago, Ill.
Dr. Montague Boyd (1921), 563 Capitol Avenue, S. W., Atlanta.
Dr. Henry G. Bugbee (1916), 2 East 54th Street, New York.
Dr. Hermon C. Bumpus (1923), 112 North Madison Ave., Pasadena, Calif.
Dr. J. E. Burns (1922), 1210 Professional Building, Kansas City, Mo.
Dr. George F. Cahill (1935), 121 E. 60th Street, New York.
Dr. Meredith F. Campbell (1941), 140 East 54th St., New York, N. Y.
Dr. Arthur B. Cecil (1921), 523 W. 6th St., Los Angeles.
Dr. Fletcher H. Colby (1931), 262 Beacon Street, Boston.
Dr. J. A. C. Colston (1921), 1201 N. Calvert St., Baltimore.
Dr. E. G. Crabtree (1924), 99 Commonwealth Avenue, Boston.
Dr. C. D. Creevy (1939), University Hospital, Minneapolis, Minn.
Dr. John L. Crenshaw (1924), Mayo Clinic, Rochester, Minn.
Dr. Harry Culver (1924), 7 West Madison Street, Chicago.
Dr. David M. Davis (1939), 255 So. 17th St., Philadelphia, Pa.
Dr. Edwin Davis (1922), 1436 Medical Arts Building, Omaha.
Dr. Archie L. Dean, Jr. (1935), 30 E. 40th Street, New York.
Dr. Clyde L. Deming (1928), New Haven Hospital, New Haven, Conn.
Dr. Austin I. Dodson (1937), 501 E. Franklin St., Richmond, Va.
Dr. Wm. J. Engel (1937), 2020 E. 93rd St., Cleveland.
Dr. G. W. Fish (1938), 755 Park Ave., New York, N. Y.
Dr. G. S. Foulds (1934), 170 St. George Street, Toronto, Canada.
Dr. Roger C. Graves (1924), 12 Bay State Road, Boston.
Dr. B. H. Hager (1930), 1136 West 6th Street, Los Angeles.
Dr. Norris J. Heckel (1938), 55 E. Washington Street, Chicago.
Dr. Alex B. Hepler (1936), 752 Stimson Building, Seattle.

Dr. Wm. P. Herbst, Jr. (1940), 1801 Eye St., N. W., Washington, D. C.
Dr. Leon Herman (1933), 801 Medical Arts Building, Philadelphia.
Dr. Charles C. Higgins (1933), 2020 East 93rd Street, Cleveland.
Dr. Geo. F. Hoch (1940), 115 E. 61st St., New York, N. Y.
Dr. C. P. Howze (1934), 1801 Eye Street N. W., Washington, D. C.
Dr. Howard Jeck (1928), 745 Fifth Avenue, New York.
Dr. Clark M. Johnson (1940), 384 Post St., San Francisco, Calif.
Dr. J. C. McClelland (1934), 170 St. George Street, Toronto, Canada.
Dr. Henry O. Mertz (1930), 1711 N. Capitol Avenue, Indianapolis.
Dr. Reed M. Nesbit (1936), University Hospital, Ann Arbor.
Dr. Vincent J. O'Conor (1926), 55 East Washington Street, Chicago.
Dr. John K. Ormond (1939), Henry Ford Hospital, Detroit, Mich.
Dr. Louis Orr, Jr. (1941), 307 So. Orange Ave., Orlando, Fla.
Dr. A. H. Paine (1922), 810 Medical Arts Building, Rochester, N. Y.
Dr. Robin Pearse (1934), 170 St. George Street, Toronto, Canada.
Dr. Geo. C. Prather (1938), 99 Commonwealth Avenue, Boston.
Dr. James T. Priestley (1941), Mayo Clinic, Rochester, Minn.
Dr. Alexander Randall (1920), 1323 Medical Arts Building, Philadelphia.
Dr. Carl Rusche (1937), 906 Taft Bldg., Hollywood, Calif.
Dr. A. J. Scholl (1926), 1930 Wilshire Blvd., Los Angeles.
Dr. Thomas P. Shupe (1921), 1600 Keith Bldg., Cleveland.
Dr. Ira Sisk (1929), University of Wisconsin, Madison.
Dr. Emerson C. Smith (1941), 1390 Sherbrooke St., W., Montreal, Canada
Dr. George G. Smith (1916), 1101 Beacon St., Brookline, Mass.
Dr. Parke G. Smith (1939), 19th floor, Union Central Bldg., Cincinnati, O.
Dr. Gilbert J. Thomas (1923), 1009 Nicollet Avenue, Minneapolis.
Dr. W. H. Toulson (1938), Medical Arts Bldg., Baltimore.
Dr. John B. Wear (1937), 616 First Central Bldg., Madison, Wis.
Dr. Miley B. Wesson (1932), 490 Post Street, San Francisco.
Dr. Wm. Niles Wishard, Jr. (1939), 1711 N. Capitol Ave., Indianapolis, Ind.
(56)

CONTENTS

First Day

May 29, 1941

1. Silent Adenocarcinoma of the Kidney with Single Metastasis to the Chest. Benjamin H. Hager, M.D., and Hans E. Schiffbauer, M.D.... 1
2. An Unusual Kidney Tumor. Gordon S. Foulds, M.D..... 9
3. Tuberculoma of the Kidney. Henry G. Bugbee, M.D..... 15

Discussion

4. Renal Pressor Substances—Their Relation to Arterial Hypertension. William C. Quinby, M.D..... 23
5. Ureterocele with Congenital Solitary Kidney and Hypertension. Vincent J. O'Conor, M.D..... 31

Discussion

6. Perinephritis and Perinephritic Abscesses. W. Houston Toulson, M.D. 41
7. Recurrent Polynephritis During Pregnancy. George C. Prather, M.D. 45
8. Destruction of Kidney Caused by Injection of Silver Nitrate. John K. Ormond, M.D..... 51
9. A New Table for Fluoroscopy, Cystoscopy, and Roentgenography. David M. Davis, M.D..... 55

Discussion

Second Day

May 30, 1941

10. Gunshot Wounds of the Kidney. A. J. Scholl, M.D..... 65
11. The Treatment of Wilms' Tumors. Archie L. Dean, M.D..... 75
12. Surgical Aspects of Polycystic Kidney Disease. George F. Cahill, M.D., and George W. Fish, M.D..... 81

Discussion

13. Indications for Uretero-enterostomy. George Gilbert Smith, M.D..... 93
14. Cutaneous Ureterostomy in Active Renal Tuberculosis. Fletcher H. Colby, M.D. 101
15. Unusual Types of Obstruction at the Ureteropelvic Junction. C. D. Creevy, M.D..... 115

Discussion

16. Endometrioma of the Ureter. Alexander Randall, M.D..... 129
17. Endometriosis of the Urinary Bladder. William J. Baker, M.D., F.A.C.S., and John I. Brewer, M.D., Ph.D..... 135
18. Ulcers of the Bladder. Montague L. Boyd, M.D..... 145

19. Solitary Tumor-like Amyloidosis of the Urinary Bladder. CARL F. RUSCHE, M.D., and SAMUEL K. BACON, M.D..... 163

20. Unusual Urogenital Carcinomata. LEON HERMAN, M.D..... 169

Discussion

THIRD DAY

May 31, 1941

21. Intravesical Resection of the Bladder Wall and Peritoneal Coat for Certain Bladder Tumors. HUGH H. YOUNG, M.D..... 183

22. Cancer of the Prostate. H. C. BUMPUS, JR., M.D..... 191

23. The Effects of Estradiol Dipropionate and Diethyl Stilbestrol on Malignant Prostatic Tissue. WILLIAM P. HERBST, M.D..... 195

Discussion

24. The Clinico-Pathologic Classification of the Tumors of the Testis in Relation to Prognosis. FRANK HINMAN, M.D., CLARK M. JOHNSON, M.D., and JESSE L. CARR, M.D..... 211

25. Bilateral Embryonal Carcinoma of the Testicle. ROGER C. GRAVES, M.D., F.A.C.S., and KNOWLES B. LAWRENCE, M.D..... 227

26. A Comparative Study of the Effect of Sex Hormones upon the Function of the Human Testes. NORRIS J. HECKEL, M.D..... 237

Discussion

27. "The Imponderables." BENJAMIN S. BARRINGER, M.D..... 251

28. The Use of Prostigmine in the Management of Postoperative Urinary Retention. REED M. NESBIT, M.D., and ROBERT H. CUMMINGS, M.D.... 257

29. An Unusual Case of Prostatic Abscess. H. G. HAMER, M.D., and WM. NILES WISHARD, JR., M.D..... 261

30. Primary Carcinoma of the Male Urethra. WM. NILES WISHARD, JR., M.D. 265

Discussion

THE AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS

FIRST DAY, MAY 29, 1941

SILENT ADENOCARCINOMA OF THE KIDNEY WITH SINGLE METASTASIS TO THE CHEST

Report of a Case

BENJAMIN H. HAGER, M.D., and HANS E. SCHIFFBAUER, M.D.
Los Angeles, California

Three years ago Dr. J. D. Barney presented before this society a case of an adenocarcinoma of the kidney with metastasis to the lung which was treated by the removal of the primary growth and a single metastasis. After an interval of five years the patient was alive and apparently in good health. A careful search of the literature at that time revealed no identical case and the paucity of occurrences has prompted us to record a somewhat similar experience.

On March 28, 1939, A., a man, fifty-one years old, white, presented himself for examination with intractable pain radiating to the scapular region. In 1931 he first noticed a small, freely movable nodule under the skin above the left nipple. There was little change in the nodule until 1937 when the nodule increased in size very rapidly and pain developed in this area. Diathermy treatments were given without relief. The tumor continued to increase in size, extending into the subscapular area.

On January 26, 1939, he was admitted to the Veterans' Hospital in West Los Angeles where an aspiration biopsy was done and a diagnosis was made of a connective tissue type tumor, probably spindle cell sarcoma. The roentgenologist's impression was a chondromyxosarcoma of the fifth rib, with probable pleural involvement. The tumor was considered inoperable, and the patient was given twelve deep x-ray treatments over the involved area. The patient states that the mass apparently grew more rapidly and the pain became more severe following the x-ray treatments. A careful physical examination revealed no other abnormalities other than an enlargement of the left anterior chest due to a regular hard fixed tumor mass, apparently having its origin in the fourth or fifth ribs in the mid-clavicular line. The mass involved the pectoralis major and minor muscles in the mid-clavicular line and extended into the subscapular area. The nipple and skin were freely movable over the tumor. The patient complained of pain on pal-

pation which radiated posteriorly along the fourth and fifth intercostal nerves. There were no palpable glands in the axilla, or the supraclavicular and infraclavicular spaces. On auscultation, there was no evidence of pulmonary involvement. Roentgenograms of the chest showed no evidence of pulmonary pathologic changes or pleural involvement. In the mid-clavicular area, over the fourth and fifth ribs,

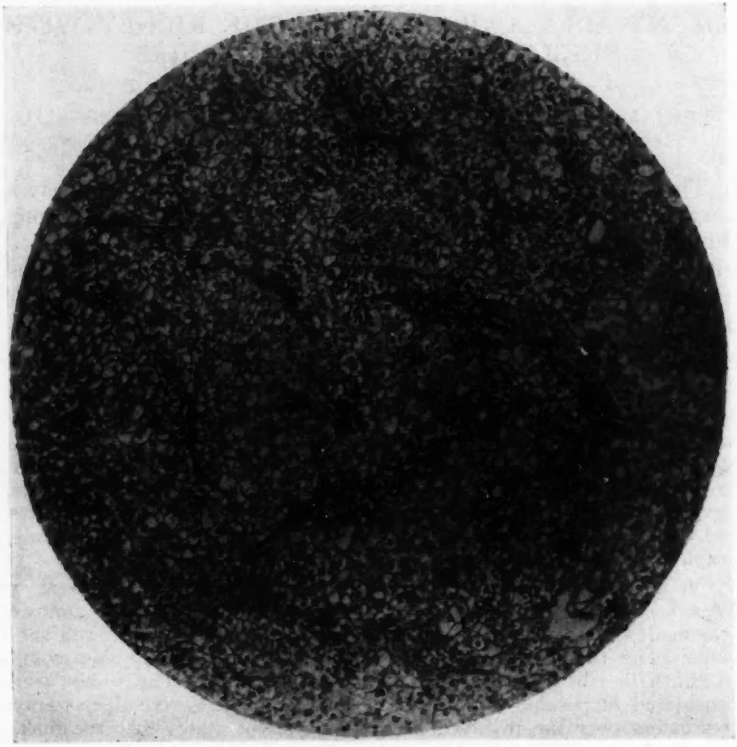


Fig. 1. Representative section of the tumor from the chest wall.

there was an increase in density with some bone destruction. There was no free fluid in the pleural cavity. The blood count and urine analysis were normal.

The patient insisted upon having the tumor removed, so as to be free from pain, disregarding all hazards of surgery. He was operated on, March 30, 1939, under positive pressure anesthesia, using nitrous oxide

ether. A large U-shaped incision was made over the chest, beginning at the costochondral junction of the second rib and continuing downward to the upper border of the sixth rib and upward along the midaxillary line to the pectoralis major fold. A skin fascia flap was dissected upward. The fourth and fifth ribs were severed at the costochondral junction, the incision carried through the parietal pleura, along

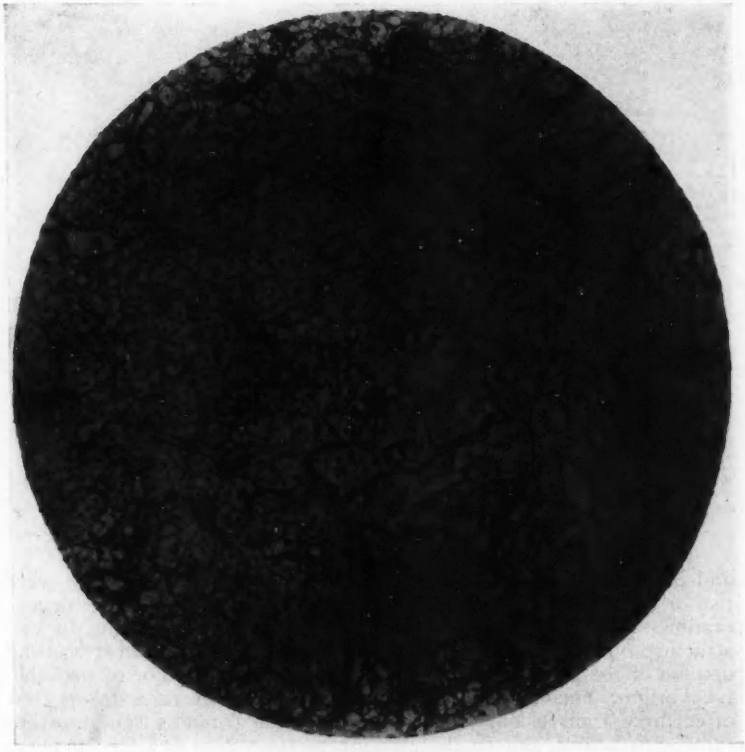


Fig. 2. Section from tumor of the kidney. Clear cell carcinoma identical with tumor removed from the chest wall.

the lower border of the third rib, to the subscapular area; the lower incision was continued along the upper border of the sixth rib and joined the upper incision under the retracted scapula. The pectoralis major and minor muscles in this area were removed with the mass. The tumor was extremely vascular and considerable difficulty was encoun-

tered in controlling the hemorrhage. No attempt was made to close the intercostal gap. After removal of blood from the pleural cavity the lung was re-inflated and the wound closed without drainage.

The specimen removed from the chest wall consisted of a moderately firm but partly softened irregular sausage-shaped mass measuring 16 x 7 cm. The tumor on section had a variegated appearance. It was generally dull, golden yellow, but mottled by many irregularly outlined

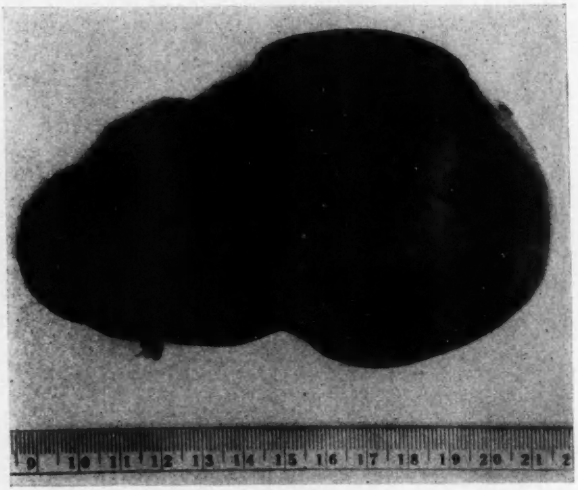


Fig. 3. Left kidney, as removed

and irregular sized hemorrhagic blotches. Near the center line were two or three cystic spaces, evidently representing areas of cystic degeneration. Microscopic section showed a tumor corresponding in cell structure type to a clear cell carcinoma of renal origin; and it was the opinion of the pathologist that this was a metastatic tumor of probable renal origin. The immediate postoperative course was quite stormy; but after three transfusions of citrated blood the patient's condition became satisfactory, and on the eleventh postoperative day the temperature, pulse and respiration were normal. Repeated urine examinations showed no abnormal findings. The patient was discharged in good condition from the hospital on the fourteenth postoperative day, his wound having healed by primary union.

He was requested to return for a kidney study in two weeks, but on April 24, 1939, nine days after leaving the hospital, he came to the office, stating that he had a sudden severe pain in the left kidney region, which gradually subsided. The pain did not radiate to the groin. The

patient definitely stated that this was the first time he had ever experienced any pain in the kidney region. Ordinarily one would have considered this pain to be due to the multiple rib resections, but because of the pathologist's report of a clear cell carcinoma tumor of renal origin, the patient was re-admitted to the hospital on April 24, 1939, and a kidney study carried out. Cystoscopic examination showed no abnormality; catheterized urine as well as urine obtained from the right

Fig. 4. Bisection of the kidney showing a well delineated neoplasm of the upper pole.

and left kidneys was essentially normal. Indigo carmine given intravenously returned in normal time and equal concentration from both meati. Retrograde pyelogram showed a normal right kidney, but in the left kidney the two upper and one middle minor calix were distorted from their usual position with a sort of hour-glass contraction of the pelvis, indicating the presence of tumor in the kidney substance.

On April 29, 1939, a left nephrectomy was done by the posterior approach. The tumor mass was confined to the upper pole of the kidney and did not involve the perirenal fat nor invade the renal vein. The pathologist's report was as follows: "The specimen consisted of a kidney, irregular in shape and measuring 15 x 10 cm. The upper pole

presented a bulbous tumefaction of rubbery consistency which was fairly well delineated. On cut section was a well marginated, but not encapsulated, spheroidal-shaped tumor situated in the upper pole. The central portion was soft and necrotic. The surface was of a golden

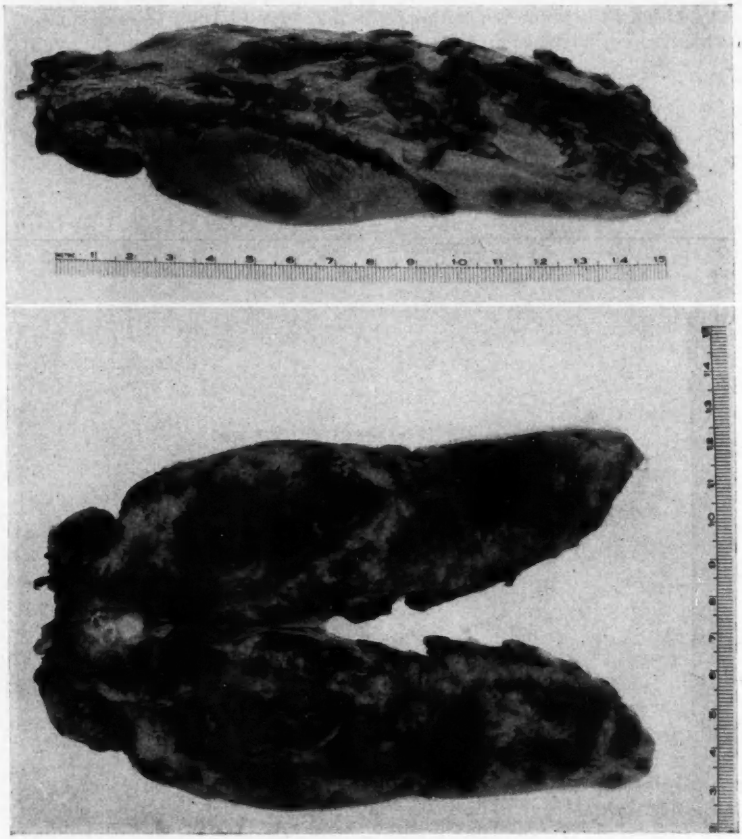


Fig. 5. *(above)* Tumor mass from the chest wall.
Fig. 6. *(below)* Bisection of the tumor mass.

yellow color and mottled red. It was of moderately firm consistency and completely replaced the kidney parenchyma in this area, being limited along most of the border by the renal capsule. The upper part of the pelvis was compressed and distorted obliterating the calices. Mi-

croscopic section showed a clear cell carcinoma identical with the tumor removed from the anterior chest." The postoperative course was uneventful; the maximum temperature was on the first postoperative day, 102.6 with a pulse of 122. The patient was discharged on the fourteenth day, in a good condition.

On May 10, 1939, the osseous skeleton was x-rayed and no evidence of metastasis was seen. On December 2, 1940, roentgenogram of the chest showed no pathologic changes. At the writing of this paper, two years and one month after the last operation, the patient was in good general health, showing no evidence of recurrent disease.

Comment.—Much has been written and many unusual experiences recorded and yet our knowledge of the biological aspects of adenocarcinoma of the kidney and its metastases are meager and vaguely correlated. A perusal of the literature affirms the vagarity of the disease. The protein nature of these manifestations imitates a multitude of disorders. Hardly a system or structure of the body appears to escape the site of secondary implants. A striking observation is the apparent not infrequent evidence of a single metastasis and the late appearance of metastasis following nephrectomy.

SUMMARY

A case is presented in which the metastatic lesion became evident eight years before the growth was extirpated. The patient is well two years after removal of the primary and secondary tumor. In all probability had our information been complete in the beginning, surgery might have been denied the patient. Our experience bears out Barney's contention—"if a metastasis is apparently solitary and accessible to surgical removal it is definitely worth-while to undertake removal of the metastasis as well as the primary growth."

REFERENCES

BARNEY, J. DELLINGER and CHURCHILL, EDWARD J.: Adenocarcinoma of the kidney with metastasis to the lung. Jour. Urol., 42:269-276, 1939.

CREEVY, C. D.: Confusing clinical manifestations of malignant renal neoplasms. Arch. Int. Med., 55:895-916, (June) 1935.

LEHMANN, VON WALTER: Hypernephrommetastasen des Skeletsystemes. Archiv. klin Chirurgie, 170, 1932.

MCCAGUE, E. J.: Fever as initial symptom of hypernephroid tumor of the kidney. Arch. Surg., 41:385-392, (August) 1940.

SCHINZ, H. R., and UEHLINGER, E.: Das Hypernephrom und seine Knochenmetastasierung. Acta Radiologica, XIV: 56-73. Fasc. 1 N; 0 77.

AN UNUSUAL KIDNEY TUMOR

MALIGNANT PAPILLARY CYSTADENOMA AND PAPILLARY CARCINOMA WITH CLEAR CELLS

GORDON S. FOULDS, M.D.
Toronto, Ontario, Canada

The origin of common renal tumors has long been a subject of debate, but in recent years there has been a growing tendency to consider the majority of them to be of purely renal origin. I wish to report a case in which a tumor was found that combined a malignant papillary cystadenoma and a small hypernephroma, because such a tumor is uncommon and because of its apparent bearing on the subject of the origin of kidney neoplasms.

Mr. F. H., aged fifty-nine years, was referred to me on December 28, 1940, complaining of pain in the left loin and discomfort during micturition. Four days previously he had had a definite left ureteral colic, followed by gross hematuria. Blood was present in the urine on two occasions. During the remaining three days there was some residual pain in the loin and dysuria, but the urine remained clear. For several years he had suffered from indigestion which was aggravated by taking of coarse or fried foods.

Neither kidney was palpable and no masses could be felt on examination of the abdomen. The genitalia were normal. The prostate was normal in size and consistency. The systolic blood pressure was 190 and the diastolic 115 mm. of mercury. The specific gravity of the urine was 1,018; the reaction was acid and a trace of albumin was present. There were one or two leukocytes and 50 to 60 red blood cells in each high power microscopic field. The nonprotein nitrogen was 39 mgms. for each 100 c.c. of blood.

Stereoscopic roentgenograms of the urinary tract showed a ring-like shadow in the right upper quadrant of the abdomen which when viewed stereoscopically appeared to be located anteriorly. No other abnormal shadows were seen. Excretory urograms were made. The dye was secreted in poor concentration on either side. The upper calices on the left side were poorly outlined. No definite conclusions could be arrived at from the urograms.

Cystoscopic examination was made on January 2, 1941. The bladder was normal in appearance. Both ureteral orifices were normal and clear urine was seen coming from each. Both ureters were catheterized without difficulty. The urine from either kidney contained an occasional leukocyte and a few epithelial cells. No bacteria were noted on direct smear and cultures remained sterile. Indigocarmine solution ad-

ministered intravenously appeared on either side in four minutes in fair concentration. Bilateral pyelograms were made, showing definite deformity in the upper calices of the left kidney (Fig. 1). The shadow on the right side was shown to be extrarenal, probably representing a gall stone.

A pre-operative diagnosis was made of left renal tumor, hypertension and cholelithiasis.

Fig. 1. Pyelogram, showing deformity in upper calix and left of kidney. A gall-stone shadow overlies the upper pole of the right kidney.

On January 10, the left kidney was explored under spinal anesthesia, through a curved left loin incision. On its posterior surface near the upper pole was a rounded cystic projection about 2.5 cm. in diameter which at first resembled a hemorrhagic cyst. This was opened. It contained a blood clot and about 3 c.c. of grumous material and was lined by villous processes. Some of the tumor material was sent for quick section and nephrectomy was done at once. The kidney was removed without difficulty and the wound closed without drainage. The patient made an uninterrupted recovery and left the hospital on the fifteenth postoperative day.

The kidney measured 13 cm. by 7 cm. by 4.5 cm. and weighed 225 grams. The outer surface was slightly roughened and reddened. The capsule was thin and stripped with difficulty, leaving a finely granular surface. In the upper pole of the kidney, projecting into a calix, there

was a soft red mass, measuring 4.5 cm. in length and 2.5 cm. in its greatest diameter. This mass had been opened to the outer surface. There was no apparent capsule separating the tumor from the renal tissue. The renal cortex measured 6 to 7 mm. and was yellowish red. The pyramids were red. The peripelvic fat was increased.

Microscopically the tumor was composed of papillary processes covered with small cuboidal cells, with deeply stained round or polyhedral nuclei. These processes projected into and nearly filled irregular cystic spaces (Fig. 2). In several of the spaces erythrocytes and (iron) pigment phagocytes were seen. The stroma was densely fibrous. In one preparation made from the material removed for quick section from the center of the tumor, small areas were found in which the cells were large and their cytoplasm clear or foamy (Fig. 3). Small blood vessels were fairly numerous and several small areas of calcification were seen. These areas, both in the character and arrangement of the cells presented a picture typical of papillary carcinoma with clear cells, the so-called hypernephroma. Preparations made from the edge of the tumor showed slight invasion of the adjacent kidney tissue. There was fibrous tissue hyperplasia between the tubules. Though the epithelium of the pelvis was reflected onto the edge of the tumor, it did not cover the projecting tumor. Sections taken from the remainder of the kidney showed little of note except that the intima of the arterioles was thickened. The pathologic diagnosis was malignant papillary cystadenoma and papillary carcinoma with clear cells.

This renal tumor contained elements of two different kidney neoplasms not usually looked upon as being closely related. The association of these distinct elements in one tumor, however, suggests a common origin for these tumors. Small renal adenomas are not uncommon findings at autopsy. They are more frequently seen in kidneys showing arteriosclerotic changes and may occur as single or multiple tumors. Figure 4 shows the microscopic appearance of one of these intracystic papillary adenomas obtained at autopsy from a patient who had had marked general arteriosclerosis with arteriosclerotic change in the kidney. There can be little doubt that larger tumors which are described as intracystic papillary carcinomas have their origin in these small adenomas.

There are very few references in the literature dealing with the transition of the malignant cystadenoma into the clear-celled papillary carcinoma of the kidney. Young described a patient from whom a papillary cystadenoma of the kidney was removed and who later developed a metastasis which on microscopic examination was a hypernephroma. More recently Trinkle, in 1936, reviewed a series of renal adenomas including thirty-seven cystadenomas. Four

Fig. 2. Section showing malignant papillary cystadenoma.

Fig. 3. Section showing papillary carcinoma with clear cells.

Fig. 4. Typical papillary cystadenoma.

of the thirty-seven showed a transition into hypernephroma similar to that found in the case which I have just reported. In 1938 Cabot and Middleton reviewed the whole subject of the relationship between adenoma and carcinoma of the kidney. They state that "the combination of tumors in one specimen, although not common, is common enough to be beyond the possibility of mere accident and quite common enough to merit speculation about a possible relation between the two lesions."

These combined tumors form a definite link between those of admitted renal origin and those clear celled papillary tumors, the origin of which has been the subject of debate since Grawitz attributed their genesis to adrenal rests in 1883 and Birch Hirschfield called them hypernephromas in 1892. Although most pathologists now agree that the majority of the tumors described as hypernephromas are really of renal origin, such cases as those of Young, Trinkle, Cabot and Middleton and the one I have reported present clinical evidence confirming their opinion.

SUMMARY

A case of renal tumor containing elements of malignant papillary cystadenoma and papillary carcinoma with clear cells is recorded. This case, with other recorded cases, illustrates the transition from renal adenoma to malignant cystadenoma and eventually, in some instances, to papillary carcinoma with clear cells.

REFERENCES

1. Birch Hirschfield, F. V.: Bret. z. Path. Ant. y.z. Allg.-Path., 24:243, 1898.
2. Cabot, H., and Middleton, A. W.: Trans. Am. Assn. G.-U. Surg., 31:91-105, 1938.
3. Grawitz, P.: Virchow. Arch., 93:39-62, 1883.
4. Trinkle, A. J.: Am. Jour. Cancer, 27:676-689, 1936.
5. Young, H. H.: Practice of Urology. Philadelphia: W. B. Saunders & Co., 1926.

TUBERCULOMA OF THE KIDNEY

REPORT OF A CASE

HENRY G. BUGBEE, M.D.
New York City

The following case is of interest as it presents a true tuberculoma of the kidney in which the urographic and gross pathologic findings were characteristic of tumor of the kidney pelvis.

The patient, Mrs. E. W., a nurse by occupation, thirty years of age, from Bermuda, was admitted to St. Luke's Hospital, January 16, 1941. Her family history was unimportant. Other than a right oöphorectomy in 1939 and a second operation in 1940, at which time a cyst of the broad ligament was removed and a ventral suspension carried out, her past history was of no importance.

The present illness began five weeks before entering the hospital when she began to have frequency of urination and dysuria. Three weeks later she had gross hematuria, hypogastric discomfort and a dull ache in the lumbar region.

The general physical examination showed no essential abnormalities. The patient was of small stature, weighing 104 pounds. The scars of the previous abdominal operations were noted; vaginal examination resulted in negative findings; there was slight tenderness in the left costovertebral angle but neither kidney could be palpated. Roentgenogram of the chest showed no tuberculosis. Blood pressure was 110/72; basal metabolism —10; blood count: hemoglobin 75 per cent; red blood cells 4,500,000; white blood cells 8,600; polynuclears 60 per cent; lymphocytes 21 per cent; mononuclears 14 per cent; eosinophiles 4 per cent; basophiles 1 per cent. Slight shift to the left. Blood chemistry: urea nitrogen 9 mgm.; CO_2 44.7; sugar 100 mgm.; blood calcium 10.8; phosphorus 4.6; phenolsulphonephthalein 64 per cent; 13, 5-4 total 86 per cent for two hours.

Cystoscopic examination showed areas of congestion throughout the bladder, no tubercles or ulceration. The bladder capacity was 5 ounces. The right ureteral orifice was normal in appearance; a catheter passed readily to the right kidney, the urine obtained was entirely normal and indigo-carmine appeared in three minutes in good concentration. The left ureter was displaced laterally. A catheter passed 1 cm. but attempts to advance beyond this point failed. The bladder urine contained pus cells in clumps and acid-fast bacilli were obtained on smear, which corresponded morphologically to tubercle bacilli.

Excretory urograms showed a normal filling of the right kidney pelvis and a normal rate of excretion. The urogram of the left kidney showed a very definite filling defect suggestive of a tumor of the kidney pelvis.

A left nephrectomy was carried out January 31, 1941, the kidney being exposed through a left oblique lumbar incision parallel to the lower border of the last rib. The kidney was not particularly adherent to the perirenal fat, was of normal size and appearance aside from a suggestion of lobulation. The ureter was not dilated or thickened. The renal vessels and the ureter were ligated and the kidney removed.

After removal the kidney was split throughout its length. The pelvis

Fig. 1. Filling defect of the left kidney pelvis due to tuberculoma.

was found to be filled with a smooth, pinkish, firm mass, which had the appearance of a renal tumor. The cortex showed good markings of the pyramids throughout and its color was normal. No areas of necrosis were observed nor were any tubercles seen. The operation was carried out before a group of twenty-two urologists, the opinion of these men being that a mistake had been made in the diagnosis of renal tuberculosis and that the pathologic change present was that of a pelvic tumor; however, a frozen section made in the operating room showed on microscopic examination that the diagnosis of tuberculosis was correct.

The pathologist's report was as follows:

Macroscopic Examination.—The specimen consisted of a kidney 10

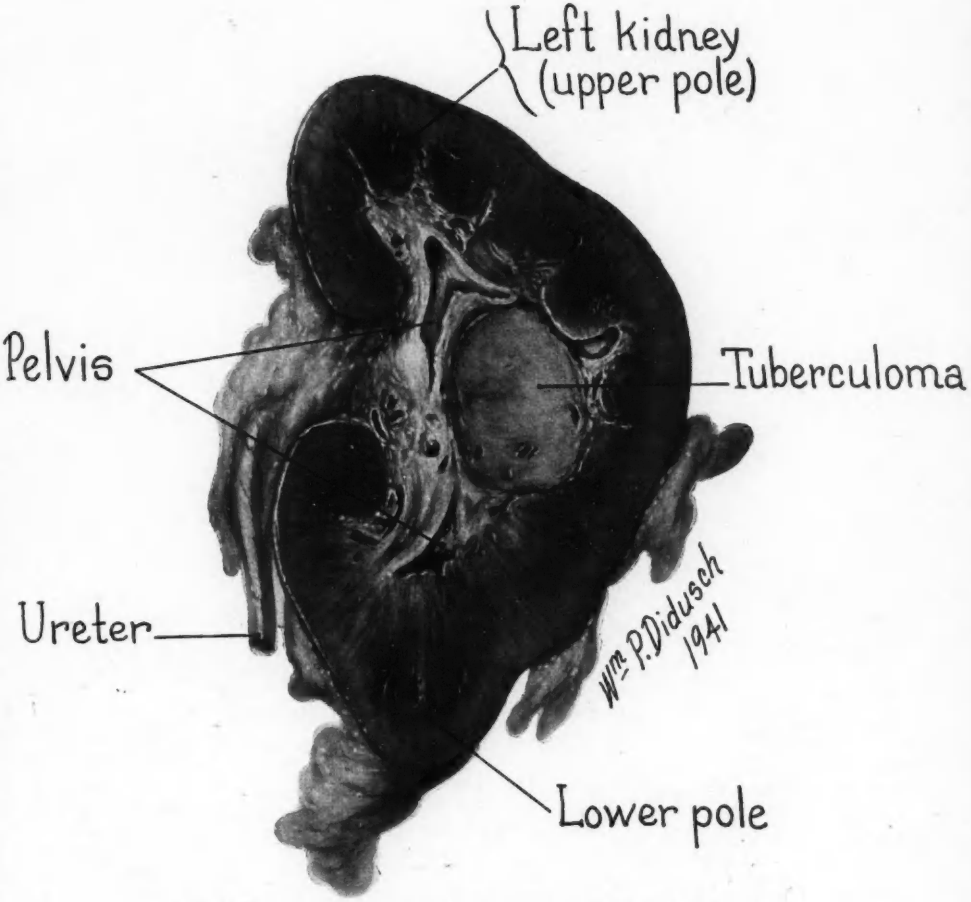


Fig. 2. Kidney after removal. Tuberculoma filling kidney pelvis.

cm. long and 6 cm. x 5 cm. at the hilum. The surface was lobulated with areas of congestion. On stripping the capsule, after the kidney was hardened in formalin, the surface was studded with yellow elevations 0.5 to 2 mm. in size. On section, the cortex was 1.5 to 2 cm. thick and in the pelvis near the center there was a sharply outlined nodule 2.5 x 2 cm. (frozen section made of this). After formalin fixation this nodule was studded with small yellow areas similar to those

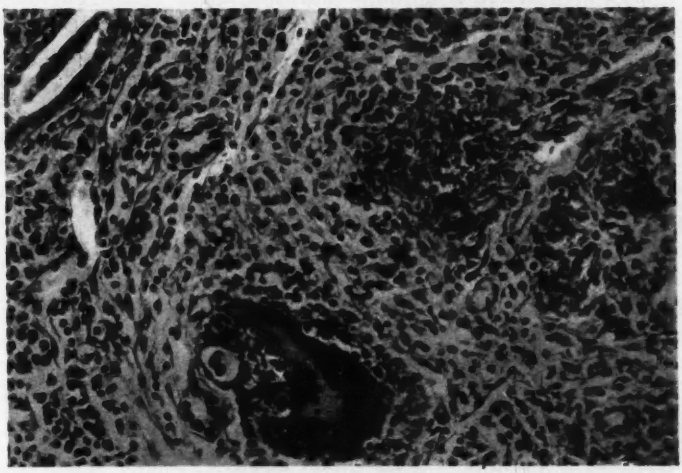


Fig. 3. Tuberculoma of the kidney. Microscopic section showing endothelial cells, lymphoid infiltration and giant cells. Magnification +150.

seen on the surface. Two centimeters of the ureter attached appeared normal.

Microscopic Examination.—Sections throughout the kidney including the large nodule in the center showed active tuberculosis, rapid formation of tubercles with many endothelial cells and diffuse lymphoid infiltration. These tubercles were confluent and discrete and were found throughout the kidney from the pelvis to the cortex. The nodules on the surface were also seen to be tubercles.

Diagnosis.—Tuberculosis of the kidney with pelvic tuberculoma.

The postoperative course was uneventful; the dysuria and frequency disappeared in two weeks and when the patient was discharged from the hospital one week later, the urine was clear.

This case represents a very early stage of the disease in which the tuberculous process presents a definite tumor formation. Necrosis and cavity formation had not taken place and although there

were definite hemorrhagic areas in the bladder, the ureter was apparently not involved. The rapidity with which the urinary symptoms disappeared and the urine became free of pus cells and tubercle bacilli following the removal of the kidney, gives ground for an excellent prognosis in such a case. The presence of pain in the flank and hematuria, also the filling defect in the kidney pelvis so well demonstrated in the urogram would have led to the diagnosis of a kidney tumor had not tubercle bacilli been found in the urine. The presence of the tuberculoma accounts for the urographic findings.

In a search of the literature we have been unable to find a report of a case of tuberculoma of the kidney. The literature on renal tuberculosis is so voluminous that it is possible that a similar case has been described in the course of some general discussion of the subject although in textbooks and the catalogue of the Surgeon Generals' Library, no reference to a tuberculoma of the kidney was found.

DISCUSSION

DR. ALEXANDER R. STEVENS (New York, N. Y.): We had an experience in New York Hospital about three years ago, which I think is of interest in speaking of Dr. Hager's case. A man came into the surgical wards with symptoms which led to a diagnosis of brain tumor. He was operated upon, a tumor removed, and the histologic report was of a carcinoma similar to the kind often found in kidneys.

The urological department was asked to investigate, although the man had had no urologic symptoms. The pyelogram gave a very clear demonstration of neoplasm of the left kidney.

The question whether nephrectomy would really benefit the patient was discussed. It seemed very reasonable to argue that if the man had neoplasm of a kidney and metastases in the brain, he must have them elsewhere; one might expect to find metastasis in the lung field, but roentgenograms of the chest showed no abnormalities. At the urging of the surgical department, we did operate, took out the kidney with the primary carcinoma, and the patient was alive two years afterwards.

DR. CARL RUSCHE (Hollywood, Calif.): I wish to present a case of silent adenocarcinoma of the kidney with single metastasis to the tenth rib in a physician, thirty-four years of age, who had a history of two months of general weakness, aching pain in the right shoulder, and afternoon rise in temperature. There were no symptoms referable to the urinary tract.

(Slide) A plain roentgenogram of the chest shows no pathologic change; however, the tenth rib on the right side is not visualized because the picture was taken on expiration.

(Slide) A plain roentgenogram of the abdomen taken four weeks later revealed pathologic changes in the tenth rib and an enlarged left renal shadow.

(Slide) The bilateral pyelogram revealed a filling defect in the left renal pelvis, suggestive of a tumor.

Neither the patient nor the family were in favor of surgery, although left nephrectomy, with removal of the metastatic lesion in the rib, was suggested. X-ray therapy was accepted and the patient

was given a total of 16,000 r units in small daily doses. Autopsy made six months following the diagnosis showed:

(Slide) Adenocarcinoma of the left kidney.

(Slide) Normal right kidney.

(Slide) Metastatic lesion in the tenth rib.

(Slide) The metastatic nodules in the liver.

At autopsy the only metastasis found were in the rib and in the liver; apparently the pathologic change in the liver was the cause of death.

I would have liked the opportunity to carry out Dr. Hager's procedure in the handling of this patient. I am sure we shall all be interested in the final outcome of Dr. Hager's patient and shall be expecting a report.

DR. GORDON S. FOULDS (Toronto, Canada): Gentlemen, within a week of coming to this meeting, a man, fifty-seven years old, was referred to me for urologic investigation. A general surgical colleague had recently removed a small nodule from the outer lower quadrant of his breast under local anesthesia. When the nodule was examined pathologically, it presented the microscopic picture of clear-celled papillary carcinoma of the kidney *(Slide)*.

No evidence could be found of any other secondary deposits, and on careful and complete cystoscopic investigation, no abnormality could be found. Both pyelograms were normal. I draw your attention to this case not only because of its interest in connection with Dr. Hager's patient, but also with the hope that I may receive some suggestion regarding the future conduct of my patient's case.

DR. LEON HERMAN (Philadelphia, Pa.): Small, silent renal neoplasms occasionally give origin to extensive metastases, especially to the lungs and spine. In rare instances, a complicating renal lesion leads one far astray. One of our patients had typical renal colic due to ureteral stone, which disappeared after instrumentation. Soon thereafter he developed hemothorax due to pulmonary neoplasm which was found at autopsy to be secondary to a small carcinoma of the kidney on the side from which the stone had come.

I have no serious objections to the use of the terms adenocarcinoma and hypernephroma synonymously, but there is a type of adenocarcinoma resulting, in all probability, from malignant changes in a benign adenoma, which is entirely different structurally

from hypernephroma. It is, too, a much more malignant neoplasm than the hypernephroma, but fortunately rare. (*Slide* showing true adenocarcinoma of kidney. Patient has survived nephrectomy ten years.)

DR. J. DELLINGER BARNEY (Boston, Mass.): I was very much interested in Dr. Hager's communication. He can tell me better than I can remember the date of this operation of mine.

DR. B. H. HAGER (Los Angeles, Calif.): It is ten years since you were up here.

DR. BARNEY: Thank you, Dr. Hager. The woman is still alive, with no evidence of metastases whatever. She had this metastasis at the time of nephrectomy. She had a large tumor of the kidney which was palpable. It was an adenocarcinoma. She had a circumscribed area about the size of a golf ball in her chest which we thought possibly was tuberculosis, because while no tuberculous sputum was found, she did have a cough and had other evidence of tuberculosis.

When it became obvious that it was not tuberculosis, we gave her deep x-ray therapy which did not improve the situation at all. So my colleague, Dr. Churchill, decided that he had better make an attempt to eradicate this growth, which he did quite easily. So far there is no evidence of metastases elsewhere and she is alive and well.

But I think it should be remembered that these adenocarcinomas of the kidney are sometimes very slow in developing and stay circumscribed and localized for a very long time. I have seen at least two cases in which we knew the patient had a tumor of the kidney for about ten years and an operation was not permitted. Finally nephrectomy was done and adenocarcinoma was found. In the meantime, they were perfectly well and had no metastases whatever. So they are slow-growing and while my case may still get metastases, I don't think it is possible at this stage of the game. Dr. Hager's patient may get metastases eventually.

Where they are accessible and where they are demonstrable, and where that is the only metastasis that is demonstrable, I think the kidney should be taken out, and the metastasis, if possible.

DR. B. H. HAGER (Los Angeles, Calif.): I want to express my appreciation to Dr. Barney because I think credit is due him for the

encouragement which he has given us in dealing with individuals who have apparently a single, solitary metastasis from adenocarcinoma of the kidney.

As one reviews the literature, it is remarkable how frequently one encounters the opinion, based on x-ray examination and autopsy, that solitary metastasis from adenocarcinoma of the kidney is neither remarkable nor unusual. That being the case, I think we should follow the advice of Dr. Barney, and when these lesions occur in a place where they can be readily extirpated they, as well as the primary lesion, should be removed.

With reference to Dr. Foulds' case, certainly the histologic structure appears like that of the clear cell adenocarcinoma of the kidney. Inasmuch as there is no evident deformity in the pyelogram and no demonstrable disease in either kidney I do not believe that bilateral exploration will be of much avail. One has to wait and watch, but in the meantime I think one is justified in removing the metastatic lesion.

RENAL PRESSOR SUBSTANCES—THEIR RELATION TO ARTERIAL HYPERTENSION

WILLIAM C. QUINBY, M.D.

From the Urological Clinic of the Peter Bent Brigham Hospital, Boston, Massachusetts

In the study of the relation of the kidney to that condition of the body known as vascular hypertension a very considerable number of experimental observations have been made of late years, the results of which may be discussed in two groups. The first group is made up of those observations showing hypertension to follow a reduction of the normal amount of blood passing through the kidney by causing a partial ischemia. In the second group fall those observations which demonstrate the production or elaboration by the kidney of substances which on injection into a test animal have a blood pressure-raising power.

Previous to the work of Goldblatt which began somewhat over ten years ago, all methods used in the attempt to create an experimental hypertension by interference in one way or another with the normal kidney, had failed entirely or had given inconclusive results. Using an especially constructed clamp by which the lumen of the renal artery could be reduced to whatever degree desired, Goldblatt was the first to produce by this method the development of a persistent elevation of the systolic blood pressure.

The results of his extensive observations are given in the Harvey Lecture of 1938 as follows:

"If the main renal artery of one kidney is constricted and the ischemic kidney is removed some time later, when the blood pressure is still well elevated, the blood pressure falls promptly to the normal level. If, instead of nephrectomy, the clamp on the one ischemic kidney is released or removed, the blood pressure also returns promptly to the original level. If the elevated blood pressure is first produced by the constriction of the main renal arteries of both kidneys, and only one clamp is released, the blood pressure falls slowly to lower or to the original level in about the same time that it does when only one clamp is applied. If in a hypertensive animal, both clamps are released, the blood pressure falls promptly to the original normal level. If one kidney is transplanted to the neck or inguinal region, and the other kidney removed, constriction of the arterial blood supply to the transplanted kidney results in the development of elevated blood pressure. Bilateral

nephrectomy is not followed by the development of persistent hypertension. These results constitute evidence that the kidney is responsible for the effect, and that it must be present in the body in order for the hypertension to occur."

All possibility of a nervous action was also ruled out and Goldblatt comes to the conclusion that these results must be due to a substance, yet unknown, elaborated by the partially ischemic kidney. Clinical observations of the hypertensive animal show further that no appreciable diminution in renal function is present if the ischemia is not too severe. In those animals in which the arterial occlusion is too great, death follows from uremia. Also in favorable experiments no change in the normal anatomic structure of the kidney is evident.

Recently Page has demonstrated another method by which hypertension can be produced in the experimental animal. The kidneys of dogs, cats and rabbits were wrapped in a surrounding layer of sterile cellophane. There follows an extensive perinephritis in the form of a layer of chronic inflammatory tissue from 3 to 5 mm. thick; and after three or four weeks there appears an elevation of the blood pressure at times even as high as 240 mm. Hg. Though in its earlier stages the resultant effect on the kidney is rather hard to relate to ischemia, later ischemic scarring is easily seen which may go so far as to cause some compression of the renal pedicle. The similarity of the local condition thus produced to those cases of perinephritis of man seen frequently by the urologist, is most suggestive. These two methods have been the most valuable up to date for producing hypertension in experimental animals.

Observations of our second group, consisting of the finding of a substance derived from the kidney which possesses pressor qualities began as far back as 1898 on the demonstration by Tigerstedt and Bergmann that a saline extract of the kidney caused a rise in blood pressure when injected intravenously into an experimental animal. This work, doubted at first, has been adequately and generally confirmed today. The supposed substance was given the identifying name of "renin." Intensive study of this substance has been attempted notably by the school of Houssay in Buenos Aires and by that of Page and collaborators as well as by many others. The prevailing opinion is that renin is an enzyme or enzyme-like substance, which acts on a globulin present in the circulating blood to form a substance having a vasoconstricting property. It is assumed that the

blood and tissues possess also another enzyme which has the power of destroying the pressure-raising substance.

Renin acts on hypertension precursor (hypertensinogen) to form hypertensin which is destroyed by hypertensinase. Evidence is also at hand which seems to indicate that the normal kidney inhibits or counteracts the action of the substances elaborated by the ischemic kidney. Page and his co-workers use the term "angiotonin" to denote the substance "hypertensin" of the Houssay school.

Thus far, therefore, have we come in the experimental laboratory toward the solution of the problem of hypertension. It may not be asking too much of us as physiologists to agree that disturbance of the renal blood flow in the direction of ischemia will result in the production of a substance, either entirely abnormal or in abnormal amount, which will pass out of the kidney to have a blood pressure raising effect by constriction of the finer arterioles of the general body. Also, in view of the large factors of safety as concerns the amount of renal tissue with which the body is endowed, it may not surprise us to find that the experimental production of hypertension does not require such a degree of ischemia as to result in reduced renal function as tested by the usual methods. But it would seem very remarkable if no histologic changes from the normal could be demonstrated in a kidney so treated. One very suggestive communication in this regard is that of Goormaghtigh, who has reported changes to be seen by appropriate staining methods in the interesting group of cells at and about the afferent artery to the glomerulus. He has pointed out definite variation from their usual appearance in these cells in animals made hypertensive by the Goldblatt clamp method. It remains for further observation to demonstrate the possible significance of these changes.

My own small contribution to this most important and interesting problem of hypertension, the result of renal ischemia, follows. Since most of the previous experimental observations have dealt with the effect of long standing partial ischemia of the kidneys, or of test animals into which various extracts of normal or ischemic kidneys had been injected, my associate Dr. Simeone and I undertook to study the immediate effect of short lasting but total ischemia of the kidney, not in a second test animal but in the same one. For this purpose, with the animal under urethane anesthesia the renal artery on each side was occluded entirely by suitable adjust-

able clamps. At periods varying from a few minutes to about five hours later, the clamps were released and the effect recorded by carotid cannula on the kymograph. One of the resulting tracings is shown in Figure 1. The rise in blood pressure following release of the occluding clamps can only have been due to some substance originating in the kidney since all other influences on the blood pressure had been excluded by carotid ligation, vagotomy, cardiac denerva-

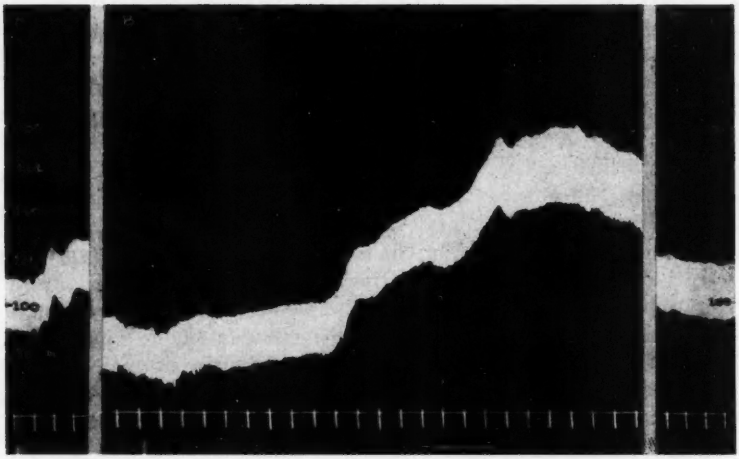


Fig. 1.

tion and adrenalectomy before making the tracing. We have here indisputable evidence of the humoral nature of the effect and a demonstration that the pressor effect can be a sequel of an acute complete ischemia as well as of the continuous partial arterial occlusion produced by the Goldblatt clamp. Our observations in this series of experiments will be reported *in extenso* elsewhere.

Clinical Observations.—Already attempts are being made to benefit patients having malignant hypertension by the use of various medicaments by which it is hoped to counteract the effect of the blood pressure-raising substance from the kidney. Space will not permit consideration of this aspect of our subject here other than to point out the fact that already the results of such treatment at various hands seem to be encouraging.

As urologists we are still actively on the watch for patients having hypertension together with a unilateral renal lesion, for whom operative removal of the diseased kidney seems strongly indicated. Each of us has probably seen an occasional patient of this sort. But not every diseased kidney is associated with hypertension and it is also equally true that frequent instances of hypertension appear in which it is quite impossible to demonstrate any renal abnormality at all by our usual method of study.

The recent report of Hines and Lander in which the blood pressure readings of 1,522 patients were compared at their second visit to the Mayo Clinic from ten to twenty years after their first record finds hypertension in approximately 15 per cent of all persons and in probably a third of all over fifty years of age. "In respect to the correlation between the original blood pressure and the subsequent development of hypertension there was little difference between the series of patients suffering from urologic disease, 264 cases, and a control series of persons who had no renal or urologic disease." This, of course, emphasizes the probable point that not all hypertension develops on a background of renal disease. There are on record, however, a number of striking cases in which removal of a single diseased kidney has been followed by undoubted reduction in blood pressure with relief of hypertensive symptoms. But there is still quite insufficient material at hand to permit judgment regarding the type of renal lesion, removal of which may be followed by the relief of hypertension. The most definitely beneficial results thus far seem to be in the cases having chronic unilateral pyelonephritis as noted by Butler. In explanation of the failure of nephrectomy to relieve hypertension there arises the question of whether the changes in the finer arterioles throughout the body which accompany the hypertension, are reversible once they have taken place, and if so, whether the duration of the existence of such changes may not be of importance. Much further information is needed about such factors.

As illustration of the seemingly belated beneficial effect of nephrectomy for pyelonephritis the following case is of importance.

A business man of forty-seven years had been known for fourteen years to have an undeveloped right kidney, infected and containing a small calculus. Also during this time he had been found, at various examinations, to have a systolic blood pressure ranging from 145 to 220 mm. Hg. Colon bacilli were constantly present in the urine from the

right kidney. The left kidney was always found normal. The infection was never so severe as to cause any abnormal symptoms on the part of the bladder and also he had never had attacks of fever or pain in the loin. The onset of the patient's complaints followed an attack of otitis media, since which he found that periods of hard work were followed by exhaustion and a very unnerved "all-in" feeling. Constitutionally the patient was of splendid physical development, but distinctly "high strung." Cessation of all work resulted in marked improvement but the attacks of exhaustion were becoming more frequent. A diagnosis of hypertensive vascular disease and unilateral pyelonephritis with calculus was made. The total renal function had always been normal. On June 14, 1938, he submitted to nephrectomy. The kidney was described by the pathologist to be of normal shape but measuring only 4.7 x 1.2 x 2.8 cm. The cortex was only 0.4 cm. in thickness. There was no dilatation of the pelvis or calices, an upper one of which contained a small stone. The ureter was of somewhat smaller size than normal. Microscopic study showed marked pyelonephritis, the arteries and arterioles showing thickening of the intima. The sequence of events was described by the pathologist to be (1) congenital hypoplasia; (2) formation of calculus; (3) pyelonephritis; (4) arteriosclerosis of the finer arterioles.

Recovery from operation was uneventful but in the ensuing months no change in the hypertension appeared, and the patient underwent several of his accustomed periods of prostration, as a result of very active work. The blood pressure also remained markedly elevated. About six months ago, however, some two and one-half years after the nephrectomy, he went through a very strenuous community-fund drive, this time without any ill effect at all, and his blood pressure is now found to average about 140 systolic. It will be of much interest to learn whether or not these favorable conditions persist.

BIBLIOGRAPHY

1. Butler, A. M.: Chronic pyelonephritis and arterial hypertension. Jour. Clin. Investigation, 16:889-897, 1937.
2. Clara, M.: Anatomie und Biologie des Blutkreislaufes in der Niere. Arch. f. Kreislaufforschung, 3:42-94, 1938.
3. Goldblatt, H.: Experimental hypertension induced by renal ischemia. Harvey Lectures, 33:237-275, 1938.
4. Goldblatt, H., and Kohn, J. R.: Effect of occlusion of ureter on experimental hypertension. Jour. A.M.A., 116:2428, 1941.
5. Goormaghtigh, N.: Histological changes in ischemic kidney with especial reference to juxtaglomerular apparatus. Am. Jour. Path., 16:409-416, 1940.
6. Goormaghtigh, N.: Le cycle glandulaire de la cellule endocrine de l'arteriole renale du lapin. Arch. de biol., 51:293, 1940.
7. Graef, I., and Page, I. H.: The pathological anatomy of cellophane perinephritis. Am. Jour. Path., 16:211-221, 1940.
8. Hines, E. A., Jr., and Lander, H. H.: Factors contributing to the development of hypertension in patients suffering from renal disease. Jour. A.M.A., 116:1050-1052, 1941.

9. Munoz, J. M. (et al.): The mechanism of renal hypertension. Am. Jour. Med. Sci., 200:608-618, 1940.
10. Page, I. H.: Newer aspects of experimental hypertension. Blood, Heart and Circulation, pp. 239-265, 1940.
11. Smith, H. W.: Physiology of the renal circulation. Harvey Lectures, 35: 166-222, 1939-1940.

URETEROCELE WITH CONGENITAL SOLITARY KIDNEY AND HYPERTENSION

REPORT OF TWO CASES

VINCENT J. O'CONOR, M.D.
Chicago, Illinois

Because of the increasing interest in the association of various urologic conditions with arterial hypertension, we feel that the following case reports merit presentation before this Association and inclusion in the literature.

Case 1.—Arnold W., aged twenty-two, was referred to us by the late Dr. Theodore Tieken on June 5, 1925. He was recently graduated from the liberal arts course of the University of Illinois. In September, 1921, upon entering the University, he had been given a thorough medical examination and it was discovered that he had a blood pressure of 165/90. The only other positive finding in the entire examination was the presence of a faint trace of albumin in the urine and a few leukocytes and erythrocytes in the centrifuged specimen. Because of these findings the family was advised that he was suffering from "nephritis" and that all unnecessary physical activity was forbidden. This patient stated that at no time in these four years had he suffered from headache, undue fatigue, dyspnea, swelling of the ankles or any noticeable physical disability. The blood pressure was observed monthly at the student health clinic and, despite his apparent physical excellence, it had gradually risen to 185 or 190 systolic and 95 to 100 diastolic. Enforced periods of rest seemed to have no beneficial effect on the blood pressure readings. The urine findings during this time varied but little except that on occasions no albumin was found. At no time had there been a febrile attack suggesting a pyelonephritis, and apart from a very occasional arising at night to urinate, there had been no urinary symptoms.

Examination from June 5 to 10, 1925 showed a well nourished male, height 6 feet, weight 178 pounds, with essentially normal findings on general examination. Vision 20/20 without correction; eye grounds normal; heart not enlarged; normal electrocardiogram.

Urine findings: There were repeated determinations of the faintest possible trace of albumin but normal concentration by Mosenthal test. Two hour phenolsulphonephthalein test showed an excretion of between 65 and 70 per cent of dye. Blood urea nitrogen 14 mg. per 100 c.c., creatinine 1.2 mg. per 100 c.c., and total non-protein nitrogen 28 mg. and 30 mg. per 100 c.c. on two tests forty-eight hours apart. The blood pressure was 182/95 on admission and varied from 190/100 to 170/90

during the five days of bed rest. Cultures of the urine on two occasions yielded no growth.

Roentgenograms of the abdomen showed nothing of note except an absence of any right renal outline and what was interpreted as a large left renal contour.

Cystoscopic examination on June 10, 1925, showed no residual urine in the bladder, an absence of anything suggesting a right ureteral

Fig. 1.

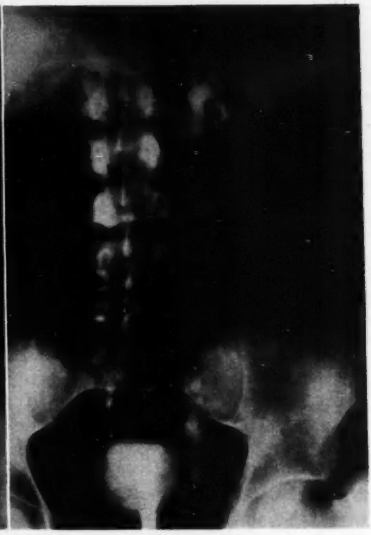


Fig. 2.

orifice (this latter search was continued after intravenous injection of indigo carmine and included a careful study of the posterior urethra as well as the bladder). Over the left border of the trigone was a large cystic-appearing protrusion characteristic of the condition called ureterocele. When this area filled with the blue urine after indigo carmine had been given, the protrusion appeared to be about 3 cm. in diameter. The ureteral orifice was in the midline of the protrusion and on the superior aspect. After some difficulty a No. 5 F. ureteral catheter was introduced and passed 30 cm. to the left renal pelvis. Ten cubic centimeters of clear urine was aspirated before normal peristaltic flow ensued. Phenolsulphonephthalein dye given by vein appeared in three minutes and 20 per cent was excreted in fifteen minutes. Pyelo-ureterogram showed a marked dilatation of the left ureter with moderate dilatation of the renal pelvis and calices (Fig. 1).

On June 12, 1925, the left cystic protrusion of the ureter was destroyed carefully with the bipolar current through the cystoscope. The ureteral orifice was then capacious enough to admit the passage of a No. 10 F. Garceau catheter with ease. On June 14 the blood pressure was 145/90 and there had been no untoward reaction from the cystoscopic destruction of the protruding ureterocele. Because of the unusual features of the problem the patient was kept in the hospital until June 20 at which time cystoscopy showed a satisfactory left ureteral orifice region. Blood pressure on this date, eight days after the original procedure, was 128/80.

The patient returned July 10, 1925, with blood pressure of 118/78. The urine showed a faint trace of albumin and 3 to 5 leukocytes and erythrocytes in the centrifuged specimen.

From July 10, 1925, to December 18, 1926, the blood pressure varied from 118/78 to 128/85 and the previous urine findings persisted. Cystoscopic examination on this date (eighteen months after cystoscopic destruction of the ureterocele) showed a rather patulous left ureteral orifice which readily admitted a No. 10 F. Garceau catheter. Repeated search for a right ureteral orifice was unsuccessful. The left pyelo-ureterogram (Fig. 2) showed a marked decrease in the diameter of the left ureter and a normal outline of the renal pelvis and calices. For the past, almost fifteen years, this patient has enjoyed excellent health, and has pursued an active outdoor life in Montana. His blood pressure reading as described to me by his family physician on April 12, 1941, was 130/90. The urine continues to show a faint trace of albumin and a few cells in the centrifuged specimen. So far I have been unable to obtain an excretion urographic study, but he has promised to have this done if he ever gets to the city.

The clinical course of this patient was a matter of great interest to us because of our previous observations on the blood pressure changes often associated with the relief of prostatic obstruction. There seemed to be some similar features in the two problems.

Case 2.—Joseph T., aged twenty-three, was referred to us by Dr. Jerry Kearns on March 4, 1938. He stated that three years before, when applying for a position as an elevator operator in a loop office building, he had submitted to a physical examination. At this time (aged twenty) he was found to have a blood pressure of 165/100 and the urinalysis showed a "small" amount of albumin with some excess of leukocytes in the sediment. During the three years prior to our seeing him, he had been carefully examined on a number of occasions by several competent internists. The blood pressure had varied from 155 to 175 systolic and 95 to 110 diastolic during this time. Retinal examinations on three occasions were described as showing no sclerosis. Blood chemistry studies on two occasions were reported as normal. His physical condition was so good and, since there had never been any

symptoms of pain or urinary difficulty, he was inclined to make little of the whole affair. However, one of the doctors in the building where he worked had made a roentgenogram of his abdomen and told him that he had a very large left renal outline, but apparently none on the right. This was verified by us at his first examination and we were immediately impressed with the similarity of his story with that of the patient seen twelve years before. We prevailed upon him to undergo a complete examination on March 6, 1938.

Fig. 3.

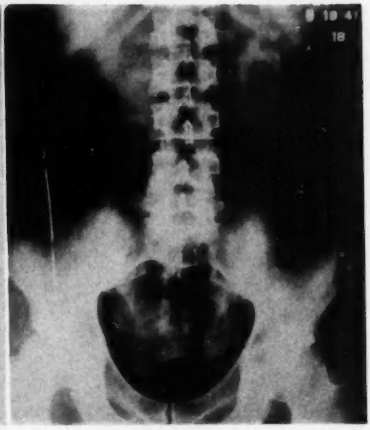


Fig. 4.

Summary of Examination.—Negative eye grounds; excellent oral and throat condition; no cardiac enlargement; normal electrocardiographic tracing, blood pressure 172/102, slightly palpable left kidney; no areas of tenderness or rigidity. Prostate per rectum normal in size, shape and consistency, with 6 to 8 leukocytes in the expressed sediment. Urine analysis showed 1.020 specific gravity, 1 mm. ring of albumin; occasional leukocytes and erythrocytes in the centrifuged specimen, no growth on culture. Blood urea nitrogen 16 mg. per 100 c.c. of blood, creatinine 1.3 mg. and non-protein nitrogen 28 mg. per 100 c.c. of blood.

Excretion urogram on March 6, 1938 (Fig. 3) showed no dye output on the right. On the left there was a dilated ureter filling to a large pouch in the intramural region of the bladder. There was a moderate dilatation of the left renal pelvis and calices. On these findings a diagnosis of probable left congenital solitary kidney with ureterocele was made.

On March 8, under intravenous Pentothal anesthesia, cystoscopic examination verified this diagnosis and the left ureterocele was seen

to be about 4 cm. in diameter. No right ureteral orifice could be found. Again indigo carmine was given as an aid. The ureterocele was incised with the Caulk high frequency knife and the loose flap-like edges coagulated by electrode. A No. 12 F. bougie could then be passed easily through the left orifice. The patient left the hospital on March 11 (three days later) with a blood pressure of 140/90. On April 3, 1938, his blood pressure was 128/90 but the urine contained much pus and yielded colon bacilli on culture. On April 20, after a course of calcium mandelate therapy, the urine was clear and sterile to culture. Repeated observation of this patient showed his blood pressure varying from 135/90 to 128/80 during the past three years. On May 19, 1941, he was examined by my associate, Dr. Sokol. The blood pressure was 128/80; his urine still shows a trace of albumin but is negative to culture. Excretion urogram (Fig. 4) shows a moderate decrease in ureteral outline but complete dye excretion in forty minutes. He is now operating a small farm and says that, while he never felt sick, he feels better than he ever has in his entire life. This latter statement may be prompted by his change of occupation.

These two similar but rather unusual patients are reported without entering into any prolonged comment. The fact that both of these young adult males had been committed to the diagnosis of "essential hypertension" or "nephritis" and that their blood pressures have returned to normal after improving the drainage from the solitary kidney is an interesting if not, at present, pertinent observation. Also the fact that normal blood pressure has maintained in one patient for almost fifteen years and in the other for over three years is evidence that the relief seems to be of a permanent nature. Since neither of these patients ever gave evidence of preexisting renal infection, this element in the etiology of the hypertension can also be discarded.

DISCUSSION

DR. GEORGE F. CAHILL (New York, N. Y.): The problem of hypertension is now of great interest. Dr. Quinby has just described the history of the steps to identify the causative agent. More recently, additional work has brought out some interesting angles.

For a long period of time it has been known that certain amino acids could be a producing cause of hypertension. Bing, using first animals' kidneys and later, recently removed human kidneys, and keeping the kidneys functioning in a perfusion apparatus has been able to show that when these kidneys were subjected to the ischemia of a Goldblatt clamp, a pressor producing amino acid was found in the perfusion fluid.

Totally independent, Schroeder, accepting the supposition that the pressor substance was an amino acid, attempted to introduce some additional substance that would de-aminize such a pressor substance and render it inert. He found, experimentally, that tyrosinase would do this in animals and later found it would also do this in a human. In other words the blood pressure in renal hypertensive cases has been reduced for periods after the introduction of a substance that specifically will render inert a pressor amino acid if such is present.

DR. G. W. FISH (New York, N. Y.): Two important contributions in the chemical warfare being waged against hypertension have recently been made, both by Dr. Henry A. Schroeder. The first was his experimental and clinical use of tyrosinase, an enzyme derived from mushrooms. The experimental work on animals was reported in *Science,* January, 1941, and in *The Journal of Experimental Medicine,* April, 1941. Seventeen human cases were treated with encouraging results. A preliminary report on these was made before the Clinical Society of Genito-Urinary Surgeons by Dr. Schroeder in January, 1941. At the present time Dr. Schroeder is working with a de-aminizing substance. Preliminary experimental work is most encouraging.

DR. A. J. SCHOLL (Los Angeles, Calif.): Doctor Jeck's paper would be a welcome addition to our discussion of hypertension and renal infarct. I regret that he is not here to present his paper.

Similar to the vascular changes following renal ischemia from other types of renal lesion, hypertension may occur late in the disease or it may be absent entirely in cases of renal infarct. In a review of thirty-five autopsies on cases of mitral stenosis, a disease in which renal infarct most commonly occurs, renal infarcts were found in nine. Hypertension had been present in seven and absent in two cases. In one of the two cases in which hypertension was not present, extensive infarcts were found in both kidneys; not only was hypertension not found, but there was no indication of left ventricular hypertrophy, even though the infarcts were apparently of long duration. In an occasional case, especially after bed rest or cardiac changes, a left ventricular hypertrophy is a better indication of the presence of long standing hypertension than is the immediate blood-pressure reading. Dr. H. A. Edmonston was one of the first to draw attention to the vascular hypertension occurring in cases of renal infarct, and he believes that the hypertension and left ventricular hypertrophy result, as may occur in cases of pyelonephritis, from renal ischemia.

Infarcts of the kidney, whether healed or not, while histologically easily distinguished from pyelonephritis, nevertheless may show extreme narrowing of the lumina of the arteries or arterioles, due to thickening of their intimas. The condition present in cases of renal infarct is not dissimilar in its relationship to hypertension to that found in cases of pyelonephritis. Weiss and Parker, in discussing the vascular lesions of pyelonephritis, state that we are dealing with a vicious circle precipitated by pyelonephritis, which is in turn accentuated and accelerated by hypertension. The fact that some patients with renal infarct do not have hypertension may be merely a question of extent and age of the infarct.

Dr. Clyde L. Deming (New Haven, Conn.): This discussion of hypertension due to renal disease I believe would not be complete without calling your attention to Dr. Winternitz's work in New Haven. Of course, we appreciate the circulatory factors which have been brought out by Dr. Goldblatt and the physiologic factors which have been brought out by Dr. Page, but Dr. Winternitz brings out the pathologic condition. He has corroborated Dr. Goldblatt's work by obstruction to the renal artery and also Dr. Page's work with the use of cellophane around the kidney.

Dr. Winternitz, it seems to me, applies his experimental work

more closely to the interest of the urologist and uses factors which are more commonly seen by the urologist. If one obstructs one renal artery, the histologic picture is one of acute necrosis with infarcts, thrombosis, in these various organs and in the opposite kidney. If one obstructs the ureter, the same pathologic picture occurs. Winternitz attacked the problem from the ureteral side and found that in obstruction of the ureter in the dog many pathologic lesions of necrosis and hemorrhage occurred in the intestines, in the aorta, in the lungs, and in the kidneys. If one obstructs both ureters, the same chemical picture occurs as is found in the obstruction of both renal arteries. There is a sudden rise of nitrogen and development of hypertension, resulting in death in five to seven days.

It seems to me that we find often in our experience obstruction to the ureter by strictures, kinks, and stones; and, if these lesions are associated with infections, we get an exaggeration of the clinical picture and also more extensive pathologic lesions. I would commend this experimental work as an added interest and an added factor in our understanding of renal disease and hypertension.

Dr. William C. Quinby (Boston, Mass.): Gentlemen, your discussion, representing the interest of all of us in this subject, pleases me very much indeed. I am also very glad that none of us agrees, because the subject is so ill-known at the present time that we cannot possibly agree. We can only observe as accurately as possible, as urologists, and record our observations.

I am sorry to have seemed to overlook the work of Dr. Bing, Dr. Schroeder and Dr. Fish, with which I am very familiar, but which it was not possible to mention in the short time allowed to a paper before this meeting.

The important point is that we must be on the lookout for all conditions in human beings which have a bearing on this exceedingly interesting subject, and by recording each experience in detail we shall soon build up a mass of facts which will without doubt be of great importance in either supporting or disproving the data derived from the experimental work of the laboratory.

* * *

These two most striking cases described by Dr. O'Conor are at the moment in direct contradiction to the experimental findings of Goldblatt. He finds that if he clamps the renal artery of a kidney by the usual method, which produces hypertension, and if at the

same time he occludes the ureter, making it difficult for the kidney to get rid of its secretion, no hypertension is produced.

But in these two cases of Dr. O'Conor the abnormality, present since birth, was such as to cause interference of ureteral function with slowly increasing severity. The very important point is that here we have a definite demonstration of the fact that release of a minimal amount of obstruction to the ureter reduced the previous hypertension. Of course, we have no way of knowing the method by which the hypertension was produced. It would not seem in either instance to be associated with ischemia of the kidney.

Nevertheless, these two cases are entirely in contradiction to the experimental evidence at hand today, and therefore are of great importance.

Dr. Vincent J. O'Conor (Chicago, Ill.): Because of our interest in the relationship of increased blood pressure in association with urinary obstruction we thought some years ago that we had come upon a very interesting observation in that we had three patients with marked hypertension and unilateral constriction of the ureter with grade 2 to 3 hydronephrosis. Following progressive dilation of the ureteral obstruction the blood pressure in these patients decreased to approximately normal. However, after following these patients for a longer period of time we found that the blood pressure gradually resumed its high level even though the ureteral drainage was maintained in an adequate manner.

There are so many factors involved in this whole picture from a clinical point of view that we felt it distinctly worth-while to report these two patients in detail and, perhaps, to point out the similar clinical picture as regards the blood pressure which prevails in some instances of vesical neck obstruction. There are many features, however, of this observation which controvert recent conceptions of the rôle of the kidney in hypertension. However, we toss them into the large hopper of experience and clinical observation, hoping that by considering all phases of the subject an occasional kernel of wheat may be extracted.

PERINEPHRITIS AND PERINEPHRITIC ABSCESSES

W. HOUSTON TOULSON, M.D.
From the Department of Genito-Urinary Surgery, School of Medicine, University of Maryland, Baltimore, Maryland

Perinephritic abscesses practically always are associated with pathologic conditions of some form in the kidney. The initiating lesion may be caused by an infection arising from the cortex alone or from a pyonephrosis.

In this series of forty-one cases of perinephritic abscess an analysis was made in order to find out how many patients had demonstrable kidney lesions.

At once it became apparent, as other writers have found, that a classification of the origin of these abscesses was essential. After a review of the literature the following simple classification of Fowler and Dorman seemed the best.

1. The cases of metastatic origin in which there was a history of a remote focus of infection.
2. Those having origin in destructive lesions of the kidney.
3. Those of rarer incidence caused by direct extension from neighboring organs.

The anatomy of the perirenal tissues and their exposure to renal infections make it seem, as Hamer suggests, that all perinephritic abscesses are secondary. Adhesions between the kidney capsule and the perinephritic tissues, a common operative finding, would lead to the belief that perinephritis, while not regularly diagnosed, is quite common.

Cabot is of the opinion that coccal infections of the kidneys are often found. It is only a step further to assume that peripheral nephritic inflammations resulting from minor renal infections not only occur frequently, but are followed by adhesions between the kidney capsule and the perinephritic tissues. Since coccal infections are often benign it is reasonable to assume that they can cause localized perinephritis or a perinephritic abscess.

In only thirteen of this series of forty-one cases could pyonephrosis or a destructive renal lesion be demonstrated. Twenty-seven were proved or assumed to have a metastatic origin; one was caused by direct extension of tissue. It is rather surprising that perinephritic abscesses do not occur more frequently with a

marked pyonephrosis. Evidently the thickened renal pelvis restrains the infection better than the parenchymal capsule does.

The focus of infection in the twenty-seven cases of metastatic origin was apparent in only ten instances.

According to the experimental injections of Mitchell, an abscess growing in size can easily dissect the extraperitoneal connective tissue and break through to the other side. However, in none of the cases in this series was the condition found to spread bilaterally. Only one patient was under ten years of age. The rarity of perinephritic abscess in children has been explained by the almost entire absence of perinephritic tissue at birth and its scanty formation before puberty.

The strangest occurrences encountered in this series were in localized perinephritic abscesses. In two instances, both of which were caused by calculi, the abscesses were completely circumscribed. In one case the stone had apparently eroded through the wall of the kidney pelvis and was found embedded in a dense mass of fibrous chronic inflammatory tissue that was evidently of long duration. The other case was a stone impacted at the ureteropelvic portion of the ureter. This stone suddenly pointed laterally and eroded through the ureteral wall near the kidney pelvis, thus causing an acute, but small, localized perinephritic abscess.

The cultures of the pus from the abscesses were not always positive. In only thirty of the forty-one cases was the culture positive. In the rest of the cases six showed no growth and in five the culture was not done. Of the thirty positive cases, twelve were from abscesses with destructive renal lesions and showed a predominant B. coli growth, while the other eighteen of metastatic origin grew staphylococci either mixed or alone. In the seriously ill patients the culture was almost uniformly a staphylococcus or streptococcus. Blood cultures were not done with sufficient regularity to be informative.

SYMPTOMS

The onset of the symptoms varied in time from twenty-four hours to four weeks before admission to the hospital, the average being between ten days and two weeks. Chills, fevers, sweats, renal pain and other symptoms were accompanied by prostration, bulging of the loin and costovertebral tenderness, and were present in practically all of these patients. Those patients who had destructive

renal lesions invariably had an elevation of the nonprotein nitrogen in the blood.

DIAGNOSIS

By far the majority of the patients had obvious abscesses requiring immediate surgical drainage. In many cases the diagnosis of the presence or absence of the renal lesion was deferred until a favorable convalescent period. Fortunately, very few of these patients presented any difficulty of diagnosis, but required repeated observations, as in all other obscure diagnoses. In two cases in this series the diagnosis was missed. In eight of these patients with abscesses resulting from metastatic causes the urine showed only an occasional leukocyte. Repeated cultures of the urine were also negative. Vermooten reported autopsy findings in a case of bilateral perinephritic abscess in which a minute histopathologic study failed to reveal any sign of infection in the kidney.

Cystoscopy and investigation of the upper urinary tract was done routinely in those cases that admitted it. In the patients who were investigated in this way with entirely negative results it was assumed that the lesions were metastatic in origin, whether or not it could be proved in the history.

Most of the cases had definite roentgen findings of a mass on the affected side, concavity of the spine, obliteration of the psoas muscle shadow, elevation of the diaphragm, and displacement of the colon and ureter. Mathe's sign of fixation of the kidney was helpful in making a diagnosis where the lesion was not fully developed; especially was this true in the cases attributable to metastatic infection. In two of the cases resulting from metastatic causes the interpretation of the pyelogram was confused with that of renal tumor and the diagnosis was made only at operation.

Usually the diagnosis was easily made in those cases showing kidney destruction on any basis, whether calculus or pyonephrosis.

In spite of the hazard of the exploratory aspiration this procedure was resorted to in two cases. A large amount of subcutaneous fat makes an early diagnosis extremely difficult.

TREATMENT

Incision and drainage were all that was necessary to effect a cure in practically all cases of metastatic origin. A few of the patients were in such poor physical condition that only incision and drainage

could be done. *It was considered unwise surgery to break up the walls of a well circumscribed abscess in order to try to deliver the kidney.*

Nephrectomy was done in five cases of perinephritic abscess complicated by renal destructive lesions, and other renal surgery was performed in the remaining eight cases of this character. This was done even though a second operation was necessary.

In the case of a recently localized perinephritic abscess produced by the calculus eroding through the upper end of the ureter, a necrotic area was left in which closure of the ureteral opening was impossible. Ample drainage was allowed and three months postoperatively this was followed by ureteral dilatations.

Where the infection in or about the kidney seemed to be subsiding, it was considered wise in an occasional patient to wait until the renal infection subsided and the perinephritic abscess localized before operating.

A carbuncle of the kidney was diagnosed at operation in only one case of this series.

BIBLIOGRAPHY

1. Beer, Edwin: Coccal infectons of the renal cortex. Jour. A.M.A., 106: 1063-1070, (March 28) 1936.
2. Bugbee, Henry G.: Perinephritis and perinephritic abscess. Amer. Jour. Surg., 26:225-261, (November) 1934.
3. Foulds, Gordon S.: Diagnosis of perinephritic abscess. Jour. Urol., 42:1-4, (July) 1939.
4. Haines, Carlyle N.: Perirenal and perinephritic infections. Penna. Med. Jour., 43:1561-65, 1940.
5. Hamer, H. G.: Perirenal abscess. Surg., Gynec. and Obst., 70:595-597, 1940.
6. Mathe, C. P.: Diagnosis and treatment of perinephritic abscess: Renal fixation. A new roentgenographic diagnostic sign. Amer. Jour. Surg., 38:35-49, 1937.
7. Mitchell, G. A. C.: The spread of retroperitoneal effusions arising in the renal regions. Brit. Med. Jour., 2:1134-1136, 1939.
8. Stevens, A. R., and McLillan, A. M., Perirenal inflammation. Surg. Clinics N. A., 20:307-321, 1940.
9. Vermooten, V.: The mechanism of perinephritic abscess. A clinical and pathological study. Jour. Urol., 30:181, 1933.

RECURRENT PYELONEPHRITIS DURING PREGNANCY

GEORGE C. PRATHER, M.D.

From the Urological and Obstetrical Departments of the Boston Lying-in Hospital, Boston, Massachusetts

After completion of a pregnancy during which pyelonephritis has been a complication, both the patient and her physician are interested in this question: Will there be a recurrence of "pyelitis" if another pregnancy ensues? An answer, not necessarily correct for one individual, can be given on a statistical basis. The probabilities of recurrence, as well as the factors that may influence a recurrence, are the purpose of this paper, data for which are derived from the records of seventy-two patients with pyelonephritis associated with a pregnancy, who later returned to hospital for one or more subsequent pregnancies.

During their first pyelonephritis of pregnancy, seventy of the seventy-two patients had pyelonephritis during pregnancy; and in two, the pyelonephritis occurred immediately after delivery. Forty-three of the seventy-two patients were in a febrile phase while in hospital, and twenty-nine were admitted or seen following their febrile attack. Approximately 58 per cent were primiparæ. We obtained a past history indicative of an inflammatory type of kidney disease in 16.6 per cent. Urinary studies demonstrated a bacillary type of infection in 91.3 per cent; Gram-positive cocci in 5.1 per cent; and mixed infection in 3.6 per cent. The clinical findings indicated involvement of the right kidney alone in 48.5 per cent; bilateral disease in 31.8 per cent; and left renal infection alone in 19.7 per cent. Cystoscopic diagnoses were made in thirty-four of the seventy-two patients.

Studies of renal function at the time of our first observations were not done routinely. Blood chemistry, which of course does not measure slight changes in renal function, was normal in forty cases.

The brief summary of the clinical data involving the initial attack of pyelonephritis in pregnancy which has just been presented offers nothing new on the subject, but the following material which shows the course of events when these women returned in a subsequent pregnancy is of interest. In approximately 65 per cent, the subsequent pregnancy was normal, with no clinical evidence of pyelonephritis. Seventeen patients (approximately 23 per cent)

Fig. 1 *a*. Para I, right pyelonephritis during the sixth month of pregnancy in 1934. Intravenous pyelogram indicates delayed secretion by dilated right kidney.

Fig. 1 *b*. As a Para II in 1938, the patient developed recurrent pyelonephritis during the fifth month. Intravenous pyelogram again indicates delayed secretion by a dilated right kidney.

Fig. 1 *c*. Four months postpartum following pregnancy in 1938. Intravenous pyelogram demonstrates prompt secretion by both kidneys with excellent anatomic recovery.

developed pyelonephritis in their subsequent pregnancies. The remainder (about 12 per cent) had toxemia in their subsequent pregnancies. The seventeen patients (23 per cent) who developed recurrent pyelonephritis had a total of twenty-two pregnancies fol-

Fig. 2 *a*. Para II, right pyelonephritis during the seventh month of pregnancy in 1936. Intravenous pyelogram indicates bilateral hydronephroses and hydro-ureters.

Fig. 2 *b*. Same patient, a Para III during 1939, developed recurrent pyelonephritis. The anatomic changes in the kidneys and ureters are nearly identical with the films taken three years previously, even though the fetal spine is to the left rather than to the right.

lowing the original pregnancy with pyelonephritis. The time interval between pregnancies was one to five years, an average of 2.8 years.

The importance of a cure of the urinary infection, either during pregnancy or the interval between pregnancies,[1,2] has been emphasized repeatedly. Likewise, the careful examination of a catheter specimen of urine by stained sediment or culture has been stressed as essential in determining the question of cure. Data from this series of cases support both contentions. Of forty-three patients in whom a sterile urine was obtained postpartum following their initial pyelonephritis of pregnancy, and who were seen in a subsequent

pregnancy, eight (18.5 per cent) developed pyelonephritis in the subsequent pregnancy. Of thirty-six patients whose urine was either still infected or unreported during the interval between pregnancies, and who returned with a subsequent pregnancy, fourteen

Fig. 3 *a*. Para I, right pyelonephritis during the sixth month of pregnancy in 1934. Intravenous pyelograms indicate typical pregnancy changes in the upper urinary tract.

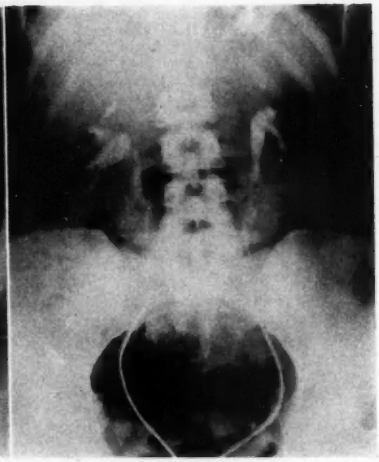


Fig. 3 *b*. Same patient nine months later. Retrograde pyelogram shows considerable resolution of the hydronephrosis and hydro-ureter.

(approximately 40 per cent) developed pyelonephritis in a subsequent pregnancy.† If we assume that at least some of the patients whose urine was unreported probably had a sterile urine between the interval of pregnancies, the rate of recurrence of pyelonephritis in women who begin their pregnancy with an infected urine would be even greater than the 40 per cent just quoted.

Thus, by and large, a woman who has had pyelonephritis associated with a pregnancy appears to have about one chance in four or five of developing pyelonephritis during a later pregnancy. The probabilities of her suffering with pyelonephritis during a later

†There is a total of seventy-nine instead of seventy-two because of the fact that a few patients had both a subsequent normal pregnancy as well as one complicated by pyelonephritis.

pregnancy are, however, greatly increased if she enters her succeeding pregnancy with an infected urine. Entering pregnancy with a latent or chronic pyelonephritis, she has only one chance in two of avoiding a febrile attack; if the pyelonephritis has been cured

TABLE I. BLOOD PRESSURE IN PYELONEPHRITIS OF PREGNANCY

	Original		Recurrent	
Case No.	Year	Blood Pressure	Year	Blood Pressure
5	1934	114/60	1938	110/70
7	1936	116/68	1939	?/?
8	1936	133/88	1938	158/108:127/78
11	1931	120/70	1936	110/70
12	1935	110/64	1937	112/88
16	1934	120/70	1936	114/64
17	1934	110/60	1938	112/80
20	1934	114/60	1938	110/70
21	1934	140/86	1938	128/80
25	1934	112/68	1936	118/90
26	1935	106/68	1937	110/80:108/90
28	1935	100/58	1939	118/60
31	1931	118/70	1936	?/?
33	1936	110/70	1938	100/58
34	1937	112/80	1939	128/80
35	1934	136/90	1937	104/72
37	1934	150/88	1938	128/80

during the interval between pregnancies, the chance of her having a febrile attack is reduced to less than one in five.

Pyelographic data were obtained in fifty-five patients, twenty-nine of whom had cystoscopy and retrograde pyelography. Intra-

venous pyelography was used in the remaining twenty-six. A few illustrations of the pyelographic studies may be instructive. Fig. 1 *a* and Fig. 1 *b* illustrate delayed secretion of the intravenous dye by the right kidney during two pregnancies four years apart, each of which was complicated by right pyelonephritis. Four months after the second pregnancy (Fig. 1 *c*) the right kidney has apparently returned to a normal state. Fig 2 *a* and Fig. 2 *b* demonstrate identical anatomic changes of the upper urinary tract in a patient whose two pregnancies were separated by an interval of three years. It is interesting to observe the same degree of ureteral dilatation in the two pregnancies even though the position of the fetal spine is reversed. Fig. 3 *a* and Fig. 3 *b* illustrate the degree of anatomic recovery which may take place following pregnancy.

With the prevalent interest in the relation of hypertension to pyelonephritis, we have noted the blood pressure readings from the charts of seventeen patients who had recurrent pyelonephritis. Although the average interval between pregnancies was not unusually long, there appears to be no tendency toward hypertension during a succeeding pregnancy as the result of pyelonephritis during a former pregnancy. The blood pressure values are recorded in Table I.

SUMMARY

In a series of seventy-two patients, recurrent pyelonephritis of pregnancy appears to have an incidence of 23 per cent. The incidence is definitely increased if the urine remains infected during the interval between pregnancies. If the urine becomes sterile during the interval between pregnancies, the chance of recurrent pyelonephritis becomes less than one in five, while if the urine remains infected the ratio becomes one in two. There appears to be no tendency toward hypertension during a succeeding pregnancy as the result of pyelonephritis during a previous pregnancy.

BIBLIOGRAPHY

1. Crabtree, E. Granville, and Prather, George C.: Urinary tract infections associated with pregnancy. Jour. A.M.A., 101:1928-1931, (Dec. 16) 1933.
2. Crabtree, E. Granville, Prather, George C., and Prien, Edwin L.: End-results of urinary tract infections associated with pregnancy. Am. Jour Obst. and Gynec., 34:405, (Sept.) 1937.

DESTRUCTION OF KIDNEY CAUSED BY INJECTION OF SILVER NITRATE

CASE REPORT

JOHN K. ORMOND, M.D.
Detroit, Michigan

Although at present, lavage of the kidney pelvis with silver nitrate solution is a much less frequent practice than in the past, this report of an exceedingly unusual result of such a procedure seems worth while.

In August, 1925, Mrs. G. L., aged fifty-four, who had been under our care for several years on account of functional gastro-intestinal disturbances and other minor ailments, was operated on by Dr. R. D. McClure for right inguinal hernia.

Following this operation she complained of dysuria and frequency and gave a history of slight intermittent pain in the left flank, dating from the birth of her only child twenty-four years before.

On examination there was found distinct but not great tenderness in the left kidney region and the urine contained pus from which on culture a growth of B. coli was obtained. Cystoscopic investigation showed the left ureteral orifice surrounded by a definitely inflamed area of mucosa, and B. coli grew from the urine from this side while the urine from the right side showed no growth. Moreover, distending the left kidney pelvis with 12 c.c. of water reproduced the pain of which she had complained.

Hexylresorcinol given orally had no effect on the infection, so about a month after the cystoscopic examination, 10 c.c. of 2 per cent silver nitrate solution was instilled into the left kidney pelvis. This was followed by a severe reaction with marked dysuria and frequency, pain in the left side, and elevation of temperature to 100°. A few days later, on attempting to pass a catheter up to the left ureter, an impassible obstruction was met at 3 centimeters from the orifice. A few days later plain roentgenograms were taken which showed the kidney pelvis outlines clearly, but rather thinly, evidently by the deposition of silver into the pelvic mucosa (Fig. 1).

During the next nine months roentgenograms were made at various times showing a gradual disappearance of this pyelogram until

finally only a small amount of opaque material remained in the neighborhood of the ureteropelvic junction and this apparently persisted.

During this period she had occasional recurrences of mild, left-sided pains running down into the left inguinal region, resembling in distribution the pain of ureteral calculus, followed by the passage in the urine of small amounts of blood and tissue. During this year,

Fig. 1. The pelvis and upper ureter on the left side outlined by the silver several days after instillation into the pelvis of 2 per cent silver nitrate.

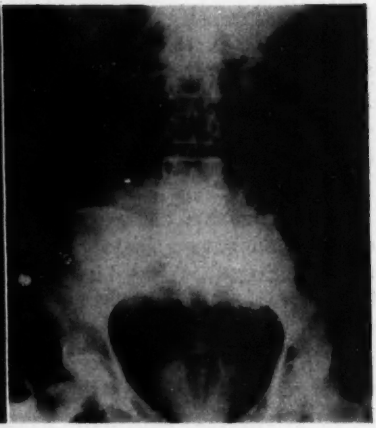


Fig. 2. Intravenous urogram. The right pelvis is essentially normal. On the left side only small shadows suggesting pelvic calculi are visible.

the urine was at times free from pus and at times contained pus in small quantities, but by the end of the year the urine-culture consistently showed no growth.†

The patient remained symptom-free until October, 1935 (nine years), when she again complained of some slight urinary symptoms which disappeared after a few bladder irrigations. In this nine-year interval cultures of the urine were made on two occasions, one culture showing no growth and the other a non-hemolytic streptococcus.

In January, 1938, she again complained of urinary symptoms and B. coli was gain found in the urine. Mandelic acid cleared this

†Up to this point this has been merely a condensation of a case report made by me and appearing in the Journal of Urology, Vol. XVIII, July, 1927, pages 91-94.

situation, but during the following three years recurrence became increasingly frequent, though each one yielded promptly to neoprontosil. These recurrent attacks of pyuria were sometimes preceded by an uncomfortable sensation, not to be dignified by the name of pain, radiating from the region of the left kidney to the inguinal region.

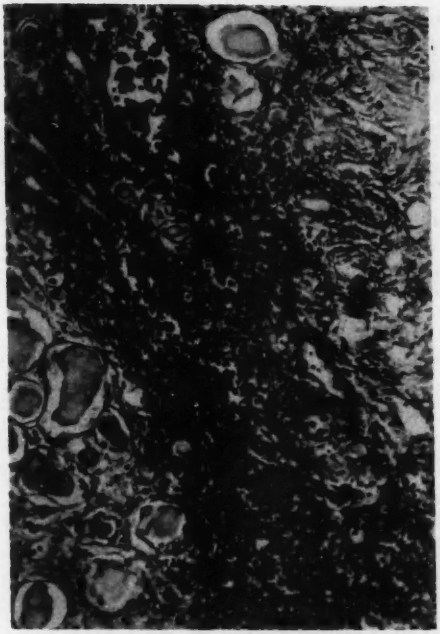


Fig. 3. Silver staining of the tissue about the left renal pelvis, fifteen years after the injection of silver nitrate.

In November, 1940, a cystoscopic examination was done. The bladder showed a mild inflammatory reaction. Indigocarmine appeared in excellent concentration from the right ureter in one and one-half minutes, and did not appear at all from the left. The urine from the right kidney contained no pus and on culture no growth was obtained. Catheters and bougies met impassible obstruction in the left ureter about 1 cm. above this orifice.

An intravenous pyelogram was made which showed a normal

pelvis and good function on the right, but no secretion and what appeared to be a small kidney on the left, with the persistence of the small shadows seen fifteen years before in the vicinity of the pelvis (Fig. 2).

We reasoned that there was a mild chronic infection in the left kidney and a strictured left ureter which at times allowed the passage of infected material from the left kidney to the bladder—causing her recurring episodes of frequency and pyuria. In view of this, nephro-ureterectomy was advised and was performed February 27, 1941.

At operation the kidney was found to be very small, about 2 inches in length, and the ureteral lumen was nearly, if not quite, obliterated. The substance casting the small shadows seen in the roentgenogram were not of silver for they did not dissolve in strong nitric acid but sections showed silver staining of the tissue about the pelvis.

DISCUSSION

Since the introduction of the new antiseptics, mandelic acid and the various sulfanilamide derivatives, the practice of treating pyelonephritis by pelvic irrigation has become less common. However, I have found pelvic irrigation with 2.5 per cent silver nitrate very valuable in controlling the bleeding in so-called essential hematuria and use this method of treatment when it is indicated. So far in those cases there have been no bad results. This case I have reported is the only one I have seen or heard of in which injection of silver nitrate caused disaster. It is a debatable question whether the silver acted directly on the pelvis or indirectly by producing a tight stricture of the ureter causing secondary renal destruction. It is of interest that there was at no time any increase in blood pressure.

A NEW TABLE FOR FLUOROSCOPY, CYSTOSCOPY AND ROENTGENOGRAPHY

DAVID M. DAVIS, M.D.

From the Department of Urology, Jefferson Medical College, Philadelphia, Pennsylvania

Fluoroscopy of the urinary tract has been little used, largely because it is difficult to carry out on account of the lack of suitable and practical apparatus. With the equipment to be found in many hospitals, it would be necessary to perform cystoscopy on one table, fluoroscopy on another, and roentgenography on a third. So much moving of the patient is troublesome for the attendants, and painful for the patient. Tables on which both cystoscopy and roentgenography can be performed are now very common, but few indeed include arrangements for fluoroscopy. The need for fluoroscopy is little recognized, even today, yet there are numerous reasons why it is greatly desirable.

In an article written twelve years ago,† I outlined some of these reasons, as follows:

"The fluoroscope offers a great deal in connection with urography. By its aid one can determine immediately the location of the catheters and their relation to any stone shadows; one can watch the pyelographic medium as it gradually fills the pelvis, massaging the kidney region, if necessary, and making certain that complete filling has occurred; and one can determine with accuracy the engagement of ureteral calculi by stone-removing instruments and see whether the calculi have been moved or extracted by these devices. Fluoroscopic examination of the patient before the instillation of the opaque medium indicates the position of the catheters and often yields information which materially changes the usual procedure. Poor position of the catheters, coiling within the kidney pelvis, or undue pressure by the tip of the catheter upon the pelvis or calix can be remedied. The opaque fluid is run in under graduated pressure and the volume and time of the filling readily controlled. The kidney and ureteral regions can be palpated under direct observation and the mobility of these organs studied in detail. The emptying time of the kidney pelvis can be studied by subsequent fluoroscopy of the kidneys every few minutes, after the catheters have been removed, until the kidney pelvis is empty. The procedure causes the patient no extra discomfort and in fact may lesson the pain frequently experienced when the pelvis is

†Davis, David M., and Warren, Stafford L.: Jour. Urol., 22:339-346, (Sept.) 1929.

over-distended during the usual method of instillation of the opaque fluid."

The publication in which these words appeared described an apparatus by means of which the patient could be moved easily from the position of cystoscopy to the fluoroscopic apparatus. This was managed by placing the patient on a flat carrier resting upon ball bearings and arranged to slide lengthwise along the cystoscopic and fluoroscopic tables, which were locked together for the purpose. While cumbersome, this apparatus functioned well.

Dr. Willis Manges, of Philadelphia, was a pioneer in fluoroscopy of the urinary tract. He designed and had made a table for cystoscopy, fluoroscopy and roentgenography. When I came to the Jefferson Hospital five years ago, I had the opportunity of using the Manges table, and renewed my enthusiasm for urofluoroscopy. Being an experimental device, the roentgenographic part of the Manges table was far from perfect, and frequently gave annoyance by getting out of order. In addition, the table suffered from a shortcoming common to all cystoscopic-roentgenographic tables; namely, that in the cystoscopic position, the patient was not in the proper position for either fluoroscopy or roentgenography, and had to be manhandled upward on the table for a distance of 3 to 6 inches.

I strongly desired to construct a new table which would avoid these shortcomings, and perhaps have some special advantages of its own. Funds were available for the purpose, thanks to the generosity of Mr. Jacob Lit, and the project met with the approval of the Board of Trustees of the Jefferson Hospital. Mr. William Hogan, of the Franklin X-ray Corporation of Philadelphia, lent himself enthusiastically to the problems of design and construction.

The central and exclusive feature of the new table is a sliding carrier, very similar to the one used by Warren and myself in 1929. The carrier is now used, however, not to transport the patient for a long distance between the roentgenographic table and the fluoroscopic table, but to permit the patient to be drawn back from the cystoscopic position at the end of the table to a point where a roentgenogram can be taken or the fluoroscope used with equal facility and perfect centering. To this end, the carrier (a) moves smoothly and easily on ball bearings, (b) has a semi-automatic stop which fixes it at any one of 8 different locations along the

tabletop, (c) is equipped with completely adjustable knee rests which do not project below the level of the carrier, and therefore do not interfere with its movements, and (d) has an adjustable clamp for a cystoscope holder so that the cystoscope can be held firmly and steadily in place while the carrier is being moved back and forth.

This carrier has also solved the problem of the drain-pan, which in older tables invariably interfered with the x-ray apparatus, since the latter had to be brought as near to the lower end of the table as possible. Now the drain-pan can be designed on generous and practical lines, as there is no need to bring the x-ray apparatus to the lower end of the table. The pan is of large size, has adequate excursion, and can be moved easily by pressure at any point along its front edge, at the ends as well as in the middle.

From a roentgenologic point of view, the table is built upon the foundation of a more or less standardized x-ray table. It rests on a heavy base, and is equipped with an electric motor which moves the table top from a 30 degree Trendelenburg position to a 90 degree upright position. The axis of rotation is so placed that the lower end of the table just misses the floor when in an upright position. There is a detachable foot rest for use when the patient is in the erect or upright position. The special feature of the table top is that there are beneath it no cross members whatever for a distance of 24 inches from the foot of the table, giving completely adequate space for the cystoscopist's knees (Fig. 1).

The fluoroscopic apparatus runs on a rail along the left side of the table, and is counterbalanced so that it can be placed wherever desired regardless of the angle of the table top. The unit is completely shockproof, the tube moves with the screen, and the shutters are actuated by double handle grips on the end of the screen near the operator (Fig. 2).

The roentgenographic tube is also shockproof and is universally adjustable upon a strong, rigid upright moving upon a floor track and an elevated guide. When the tabletop is level, or nearly so, the tube is easily and quickly centered over the film by means of scales attached to the elevated guide and to the frame of the table just under the cassette holder. The cassette holder and Bucky diaphragm are counterbalanced, so that they slide easily out of the way when one wishes to use the fluoroscope. When the cassette holder is pushed home, it and the Bucky diaphragm are raised auto-

matically against the lower surface of the table top, in order to bring the film as close as possible to the patient. Automatic exposure and Bucky timing devices are, of course, included.

The operation of the table is extremely simple. The fluoroscopic screen and roentgenographic tube are pushed out of the way. The carrier is brought to its highest position near the head of the table. The right knee rest is removed from its socket. The patient then

Fig. 1. Table in cystoscopic position. Note large pan, clamp for cystoscope, adjustable knee crutches.

Fig. 2. Table in fluoroscopic position. Note that carriage has been drawn back 18 inches from foot of table. Upper tube, Bucky diaphragm, and cassette can be quickly substituted for taking roentgenograms.

lies upon the carrier, or is lifted on it from a stretcher. The right knee rest is then replaced, the patient centered, his knees placed in the rests, and the latter adjusted to the desired position. The knee-rest supporters can be lengthened or shortened, moved laterally upon the round bar at the foot of the carrier, or put at any one of four different angles, from vertical to almost horizontal. The carrier, with the patient lying comfortably upon it, is run to its extreme position at the foot of the table, and cystoscopy carried out in the usual manner (Fig. 1). When the catheters are in place, the

cystoscope is supported by a clamp, which also has clips for holding the test tubes which contain the ends of the catheters. (The sheet used to cover the patient must have a small hole to permit the passage of the clamp.) The carrier, with patient, clamp, cystoscope and catheters, is then slid back about 18 to 24 inches. Experience shows that if the cystoscope is held absolutely motionless in this manner, pain is reduced to the minimum. The fluoroscope is brought into position, and the room darkened (Fig. 2). A small, sterilizable lamp may be attached to the cystoscope holder, and illuminated by attaching to it the cystoscopic cord. This gives a subdued light where needed to inspect the connections between the ureteral catheters and the syringes or burettes used for injecting the pyelographic medium. The injection is controlled by fluoroscope. When it is complete the fluoroscope is pushed aside, the tube stand and Bucky diaphragm drawn into place, and the desired roentgenograms made. Fluoroscopy or roentgenography can be carried out in the erect position if desired. All of this is accomplished without any jerk or jar to the patient, and, unless the erect position is used, without altering in the slightest his position on the carrier.

The tube carrier is so constructed that a rotating anode tube can be used, if desired.

While the table is still new, sufficient experience has already accumulated to show that with it examinations can be carried out with ease, satisfaction, and comfort to the patient never before realized.

DISCUSSION

DR. GEORGE R. LIVERMORE (Memphis, Tenn.): I would like to report a case of sulfathiazole in the tubules of the kidney with complete blockage, and the subsequent death of the patient. Whether it was due entirely to the sulfathiazole or whether the toxic condition, from which the patient suffered prior to its administration, caused the kidneys to stop functioning, I don't know, but anyway they stopped functioning, and the patient died the fifth day after his entrance to the hospital.

The patient was a man, forty-two years of age, admitted on May 17, with a history of chills and fever two days before and pain over his right kidney. He was seen by an internist at that time who obtained a history of chills, nausea, vomiting, general malaise, and weakness. Physical examination was negative except for an acute nasopharyngitis; hence a diagnosis of "flu" was made. He had had massage of the prostate for chronic prostatitis the previous day and was given 1/10 c.c. vaccine (staphylo-bacterin mixed). The edge of his spleen was slightly palpable. He had tenderness over his right kidney. The medication consisted of sulfathiazole, two 17.5 grain tablets, q 4 h, until he had taken 205 grains.

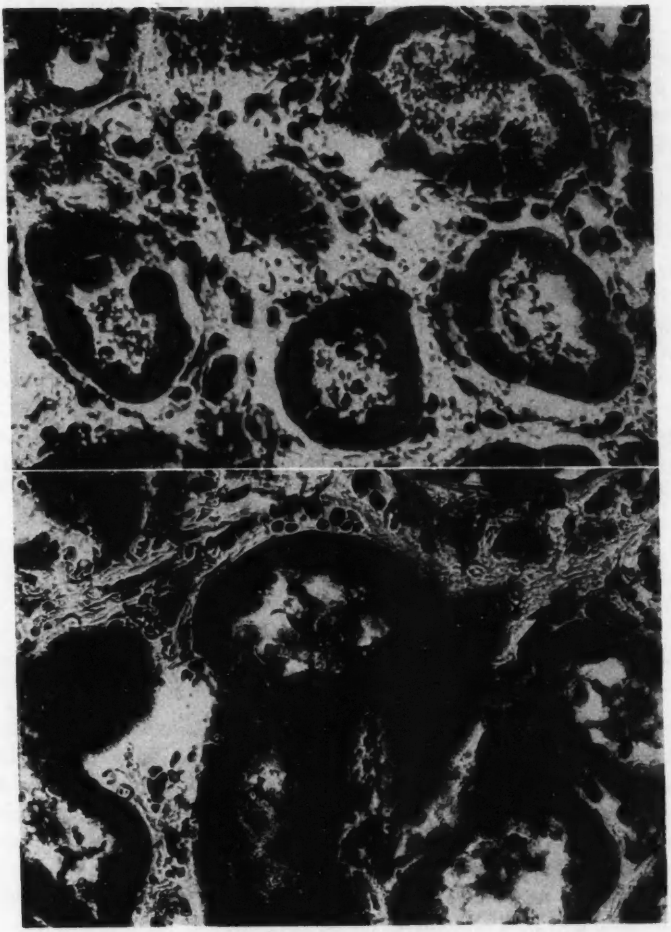
His urinalysis on admission was negative, except for a faint trace of albumin and rare pus cells. His blood pressure on entrance was 120/70. This patient had every test, I guess, that one could possibly make on him. The internist had it done before I came in. His blood count was 4,280,000 reds, and white blood cells, 5,700; polymorphonuclears, 70 per cent; eosinophiles 1 per cent; malaria, negative; hemoglobin, 84 per cent.

The next day, the test for undulant fever was negative, and his white blood cells were 7,350. His blood cultures were negative, his icteric index was 2, there was no tularemia, no typhoid and no paratyphoid. His blood cultures were negative up to the time of his death, which was on the fifth day.

The smear from his throat showed pneumococcus and Staphylococcus aureus. On the 18th, his red cell count was 5,140,000, and his white cell count was 9,250.

Two days before his death, I was called in. He had not passed any urine that day, and only five ounces the day before, so we

passed ureteral catheters and got some urine dripping from each kidney. We had cultures made and the cultures were negative. There were some fine, gritty particles in the drip from each kidney.



Figs. 1 and 2.

The catheters were left in and drained only three ounces in twenty-four hours, when the catheters slipped out. His blood pres-

sure had gradually risen. He died the following day, having passed no urine since the catheters came out.

May I show these two slides, to demonstrate the fine particles, filling the tubules of the kidney? (Figs. 1 and 2.) If you will note, the particles are completely filling the tubules. They were amorphous and not crystalline, and we never got but the three ounces of urine after the catheters were used. Every means was used to promote diuresis.

Autopsy showed toxic nephritis, with the tubules of the kidneys, both descending and collecting, choked with fine amorphous particles. The kidneys are now being examined to determine the chemical composition of the amorphous particles.

DR. REED M. NESBIT (Ann Arbor, Mich.): I wish to discuss Dr. Toulson's paper on perinephritic abscess and reiterate two points which we have previously emphasized in publications on this subject.

First, a diagnostic sign which was first pointed out several years ago to us by one of our interns, Clifford Keene. He found that râles are present at the lung base on the affected side and since this observation we have found that this diagnostic sign has been positive in 100 per cent of cases. It has been of diagnostic value in many instances.

The second point is that in a considerable series of perinephritic abscess cases which we recently reviewed, we found that 16.5 per cent had positive x-ray signs of inflammatory change, either in the pleura or the lung on the side of the abscess. Some of the changes which have been observed clinically have led to delay in diagnosis as well as treatment.

DR. LEON HERMAN (Philadelphia, Pa.): Apparently very few urologists are familiar with the table presented in 1925 by Dr. David Bowen and myself and described in the *American Journal of Roentgenology*. I doubt if Dr. Davis has ever seen the table which is much simpler, and I believe more practical than the table presented today, which, nevertheless, has certain advantages. Our table is a square table modified by the addition of an oil-immersed fluoroscopic unit and a displaceable Bucky diaphragm. The apparatus is so constructed that it may be moved in any desired direction without interfering in any way with the use of the table for complete cystoscopic procedures. We have made the Bucky apparatus dis-

placeable instead of the patient. This table has been in daily use since 1925 and is most satisfactory. The gynecologists use it routinely when performing the Rubin test. When we return to Philadelphia, I shall invite Dr. Davis to inspect our table.

Dr. Homer G. Hamer (Indianapolis, Ind.): I wish to speak to Dr. Toulson's paper on perinephritis and perinephritic abscesses, particularly as to the source of infection in these cases. He has stressed the fact that they are generally secondary to pre-existing disease in the kidney; lithiasis, tuberculosis, pyonephrosis, or metastatic infection to the cortex, or the perinephrium.

In our study of a series of cases several years ago, we formed the opinion that the majority of those cases listed as metastatic were metastatic to the cortex of the kidney rather than to the perinephrium. In a few instances, it is probable that a metastatic infection may lodge in the perinephrium proper, yet at operation it is so difficult to find a primary lesion that could be diagnosed as a cortical lesion that there is some uncertainty.

Bugbee has already called attention to the fact that in these cases, the cortical disease, or small cortical abscess which ruptured into the perinephrium may have had time to heal by the time the perinephritic abscess has developed, and are not discovered at operation.

Dr. William J. Baker (Chicago, Ill.): Since Dr. Prather has done so much work on pyelonephritis during pregnancy, I wonder if he ever worries about the bad effects upon the fetus of the multiple exposures of x-ray necessary in obtaining intravenous urograms.

Dr. W. Houston Toulson (Baltimore, Md.): Some years ago Dr. Vermoten in South Africa reported a case of bilateral perinephritic abscess that came to autopsy, and when it did come to autopsy, serial sections of the kidneys failed to show any sign of any disease. I feel as Dr. Bugbee does, that more than likely many of these diseases have had a chance to heal during the process of the formation of the perinephritic abscess.

I can say that in this one case of carbuncle kidney in this series, all that was done was a simple drainage of the perinephritic abscess; subsequent pyelograms showed an uninfected and perfectly performing kidney. I assume that the carbuncle which was absolutely

untreated at the time of operation rapidly healed from the drainage of the perinephritic abscess.

DR. GEORGE C. PRATHER (Boston, Mass.): I have no remarks to make, except in answer to Dr. Baker's question, to which we may say that we have no hesitancy whatever in using either retrograde or intravenous pyelography during pregnancy. I should qualify that statement, I think, to say that I never like to do pyelography in patients during the first month of pregnancy.

The animal experimental work in regard to the effect of x-ray on distorting the fetus no doubt led to the conclusion that it was only during the very early part of the pregnancy that any change in the fetal construction was established because of x-ray. The opinion is further substantiated by going over the fetal mortality of the patients whom we have seen with various kidney disabilities during pregnancy, who have had pyelography, in which there is no higher a mortality rate, and no higher an incidence of congenital deformities, than in the average.

DR. DAVID M. DAVIS (Philadelphia, Pa.): Here is some chronology. The original carrier table constructed by Dr. Stafford Warren of Rochester and myself was worked out during the years 1927-1928, and finally reached publication in September, 1929.

In the autumn of 1930, Leon Herman very kindly invited me down to the Pennsylvania Hospital to see his table, which I did see at that time. He was very kind and demonstrated two or three cases on it. As a matter of fact, the table which I showed today utilizes exactly the same principle of moving the Bucky diaphragm and cassette holder back toward the head of the table to permit use of the fluoroscope, the patient remaining motionless during the entire x-ray procedure.

The only thing for which I can possibly claim originality is the sliding carrier for the patient and in this table, as I said, it is used merely to obviate the necessity of trying to design the x-ray apparatus so that the lower edge of the film will be within an inch or two of the lower end of the table. This is extremely difficult from the constructional point of view, and as a matter of fact, it has never been successfully accomplished with any table. So with every table I have ever used, or seen used, it is necessary with the great majority of patients to pull them upward on the table after the cassette is in place, and before taking the roentgenogram.

SECOND DAY, MAY 30, 1941

GUNSHOT WOUNDS OF THE KIDNEY

A. J. SCHOLL, M.D.
Los Angeles, California

Gunshot wounds of the kidney caused by either bullets or shrapnel are most commonly found in conjunction with more frequent and serious wounds of adjacent viscera, and may be readily overlooked. While injuries of either abdominal or thoracic viscera usually overshadow and at times detract attention from the renal lesion, prompt and efficient treatment of the kidney wound may prevent grave disability and possible loss of life in an important group of cases.

Statistical reports from different countries vary widely with regard to the incidence of war injuries, but agreement is general concerning the rarity of uncomplicated renal lesions and the high mortality in complicated cases. Laewen[5] reported thirty-four cases of gunshot wounds through the abdomen and kidney treated in German hospitals; only three were cured. He stated that all seven cases of intraperitoneal gunshot wounds of the kidney with associated liver or intestinal injury, reported by Most,[5] died and that only two of sixteen intraperitoneal gunshot wounds of the kidney reported by Burkhardt and Landois[5] were saved. Of a total of fifty-seven cases collected and reviewed by Laewen,[5] there were only five cures, giving a mortality of 87.7 per cent. In contrast to this exceptionally high mortality, the results of treatment in British war hospitals are more encouraging. The reports of Wallace,[6] Lockwood,[3] Fraser,[1] and Walters,[7] published in 1917, and later reviewed by Young for the Surgeon General's report, covered a series of 2,121 cases of gunshot wounds of the abdomen. The kidney was involved in 155 (7.3 per cent) of these cases; 57 per cent of the patients died. In sixty-nine uncomplicated wounds of the kidney, the mortality was only 14 per cent. In the American Expeditionary Forces there were 2,385 cases of gunshot wounds of the abdomen. It is stated in the Surgeon General's report that the kidney was involved in 129 (5.44 per cent) of these cases. The mortality rate of injuries to the kidney in this group, both complicated and uncomplicated, was 55.8 per cent.

PATHOLOGY

Gunshot injuries of the kidney are classified as wounds of the parenchyma and wounds of the hilum.

The most common wounds of the parenchyma are of the perforating type; though furrows, complete destruction of either pole, or extensive shattering of the kidney may occur. A moderate number of parenchymal wounds are slight, especially those in which the edges or poles are injured. When the center of the kidney is injured, the damage is usually severe. The nature of the projectile has little particular effect on the injury, though bullet wounds destroy an area of parenchyma only slightly larger than the size of the bullet, while shrapnel makes a more irregular wound with greater destruction of tissue. In shrapnel injuries, the edges of the wound are more likely to be contused, and the adjacent parenchyma may become necrotic due to arterial injury. Many parenchymal wounds also involve the calices, but urinary extravasation is not usual unless the wound is large and extends into the pelvis of the kidney itself. If urine escapes from the wound of entrance, it is probable that the pelvis or ureter has been injured.

Peritoneal tears are common, and intraperitoneal hemorrhage or urinary infiltration into the peritoneal cavity is found in many cases.

The minor lacerations and contusions of the kidney not uncommon in civil life, while probably of high incidence in war injuries, rarely receive treatment, as they are overshadowed by other lesions or are disregarded by the patient or surgeon. Nevertheless, it is important that the surgeon bear them in mind, because they may simulate extensive renal damage but rarely require intervention. In some contusions hematuria may be quite severe; but in the absence of shock, or when there is evidence of perirenal bleeding, watchful waiting is the most desirable course to follow.

SYMPTOMS AND DIAGNOSIS

The location of the wound and the presence of hematuria are the first indications of renal damage in most cases. In uncomplicated kidney lesions the general condition is usually good. There is partial fixation and rigidity of the abdominal wall, and tenderness on abdominal palpation over the injured kidney and in the corresponding costovertebral region.

Shock is usually, though not always, present. In uncomplicated cases it is generally not severe and depends to a certain extent on the amount of blood lost. In cases with an associated injury to the abdominal viscera, thorax, or spine, shock is usually marked; though even in uncomplicated renal injuries, it is not always an accurate index of the degree of renal damage.

Hematuria, varying from microscopic amounts to massive hemorrhage, is present in most cases, though it may not occur immediately. In the early stages it is not excessive, and after several days it tends to cease spontaneously. If the wound involves only the parenchyma of the kidney, hematuria may be slight or absent.

In all wounds of the renal area, the urine should be examined for microscopic blood. If necessary, catheterization should be done, as retention is common in cases of renal injury and may be due to a concomitant cord lesion. Retention occurred in eight of forty-two cases observed by Fullerton;[2] in six of the eight, it was secondary to spinal injury. Absence of hematuria may be due to division of the ureter, to obstruction of it by blood clots or fragments of renal tissue, or to extensive damage to the renal pelvis.

Secondary hemorrhage into the bladder is of fairly frequent occurrence and is most common in the second or third week but may appear as late as two months after injury. It is not unusual that these late hemorrhages may be so severe as to cause death. Consequently, it is desirable, even in cases with only slight renal injury, as advised by O'Conor,[4] to keep the patient absolutely quiet, preferably at rest in bed if possible for at least two weeks after injury. Secondary hemorrhage may be spontaneous, or it may be an exacerbation of persistent primary hemorrhage. Differing from the primary bleeding, it is often accompanied by clotting of blood in the bladder.

Urinary extravasation in the renal area is generally not marked and is usually seen in cases of extensive pelvic or ureteral tears. Urinary infection occurs frequently and early, even when the renal damage is only slight or moderate. In many cases it persists long after renal repair has been established.

Roentgenograms give definite diagnostic information relative to the state of the kidney and should be taken as soon as possible, as gas distention develops quickly and obscures the renal outline. A plain roentgenogram of the kidney may be done in the presence of

extensive secondary injuries which prohibit more detailed urologic studies. Haziness of the renal outline, obliteration of the psoas margin, or deviation of the spine away from the injury suggests perirenal bleeding.

Excretory urography, in the presence of trauma, shock, and lowered blood pressure, usually offers but little diagnostic assistance. There is rarely time or opportunity for its use in war hospitals, and when it has been employed in cases of gunshot wounds of the kidney in civilian hospitals, even under the most satisfactory circumstances, the results were inconclusive.

Cystoscopy, ureteral catheterization, and retrograde pyelography may sometimes be necessary to establish the diagnosis. However, lack of time or equipment usually prohibits these procedures in the early days after injury. Moreover, cystoscopy is usually hazardous in the presence of shock or extensive bony lesions. Exacerbations or recurrence of bleeding may occur from shifting the patient's position or, more rarely, from instrumental manipulations. In cases where cystoscopy is indicated and can be carried out, and time and condition of the patient permit, it should be done.

In the majority of cases of gunshot wounds, particularly those seen in front line hospitals, the finer points of diagnosis obtainable by complete cystoscopy are time-consuming and unnecessary. In fact, only very rarely is cystoscopy carried out in these cases even when seen in civilian hospitals, with sufficient time, opportunity, and satisfactory equipment. The immediate questions to be settled are whether operative intervention is imperative, and whether the opposite kidney is capable of sustaining life in the event that nephrectomy is obligatory. Physical findings, wound of entry, pain, swelling, and hematuria generally determine the diagnosis and the location of the lesion.

In these cases where satisfactory uretero-pyelograms are obtained, the visualized changes in the course of the ureter and the outline of the renal pelvis give accurate information concerning the pathologic charge present. Deviation of the ureteral outline toward the vertebral column, upward displacement of the uretero-pelvic juncture, and narrowing of the calices suggest perirenal extravasation.

TREATMENT

In most cases of gunshot wound, care of the renal condition is less urgent than that of complicating lesions, and in a large proportion of cases only conservative local treatment is necessary.

Renal injury is characterized by hematuria and internal hemorrhage. Shock, common in war wounds, is rare in uncomplicated renal injuries, and should be treated symptomatically. In cases where it is due to renal bleeding, exploration of the kidney is indicated.

Hematuria, even though marked, is not sufficient reason for early exploration. Primary hematuria usually subsides in from twenty-four to forty-eight hours, but if it persists and is profuse, the kidney should be explored.

Urinary extravasation usually calls for early and extensive incision and free drainage of the area. In cases of doubt as to whether to open the abdomen or the renal area, usually the lumbar region should be explored as it involves the lesser risk, and if necessary the abdomen can be examined through the same incision. An adequate lumbar approach permits evacuation of clots, thorough visualization of the kidney, and opens an easily drained area that may be securely packed if necessary. After completing the repair of the kidney, the peritoneum should be opened in the anterior part of the incision and the adjacent viscera examined. This is important as the peritoneum and its contents are also injured in most cases of kidney wounds.

In cases where a primary abdominal exploration is performed and renal damage is probable, the kidneys should be palpated. In some cases positive information is obtained by this route, but if injury is present, usually an obscured field due to perirenal bleeding makes it difficult to determine the extent of renal damage, even if the posterior layer of peritoneum has been opened over the renal area. Exploration of the renal area transabdominally is not advisable, as it opens up a poorly drained area which is readily contaminated from the usually present abdominal infection. If, during abdominal exploration, a hematoma or obvious renal damage is found, it is unwise to open the posterior peritoneum for either further exploration or evacuation of clots. For the same reason, transabdominal nephrectomy should not be done.

When conditions found during the course of laparotomy indicate

that exploration of the renal fossa is necessary, a second incision should be made, using the lumbar approach. It is preferable, however, to postpone renewed intervention for several days, as this delay provides time for the patient to recover from shock, for his general condition to improve, for diagnostic study to be made, and in most instances for reduction of free hemorrhage in the operative field to take place. On the other hand, early exploration is imperative in cases in which bleeding from the kidney is excessive, even though it may have incited considerable shock.

Combined wounds of the kidney and liver, while serious, usually require only conservative management, and frequently surgical intervention is neither advisable nor necessary. Wounds of the diaphragm encountered during exploration of the renal area rarely require repair.

In the treatment of kidney wounds, there are three possible surgical procedures: (1) drainage of the renal area, (2) partial nephrectomy and repair of the injured kidney, and (3) nephrectomy.

1. *Drainage of the renal area* permits inspection, evacuation of blood clots, and control of bleeding. This is the simplest procedure and may be done very quickly with only slight risk to the patient. Foreign bodies and fragments of shrapnel should be carefully searched for and removed. All loose fragments of tissue should be taken out.

Drainage is indicated in cases in which time or the condition of the patient has not permitted complete studies to determine the condition of the opposite kidney. If hemorrhage is encountered, an effort should be made to control it with catgut ties or sutures. Usually there is a general oozing which does not permit complete localized hemostasis and which is best controlled by packing with iodoform or plain gauze. Lumbar incision permits firm packing, and sufficient gauze should be used to control all bleeding. Lockwood[3] advises spreading a piece of rubber dam or similar material in the wound before packing to facilitate removal of the gauze and to prevent recurrence of bleeding when the gauze is taken out.

When lacerations of the kidney are severe, and when the patient is in a precarious condition, thorough packing controls the hemorrhage until the patient is better able to stand nephrectomy.

When the kidney is not removed and drainage is installed, it should be continued until at least the tenth postoperative day.

2. *Partial nephrectomy, renal repair, and plastic operations* are frequently employed with good results in closed civilian types of renal rupture, but these procedures are usually unsatisfactory in infected, penetrative wounds. This is especially true in soldiers entering the hospital in shock after long periods of exposure. In cases where partial nephrectomy or suture has been done, parenchymal infection, necrosis, and late bleeding usually necessitate reopening the wound later, and in some cases nephrectomy.

The control of hemorrhage usually calls for surgical intervention. A partial operation is not likely to remove the cause of the bleeding, and a patient already anemic should not be exposed to the risk of a fresh hemorrhage from a sutured or a partly resected organ. Rarely are limited operations justifiable.

3. *Nephrectomy* should be done in cases with persistent hematuria, multiple deep lacerations of the parenchyma, or damage to the vascular pedicle. A patient with complete rupture of the vascular pedicle rarely reaches the operating table in a condition suitable for operation.

When the ureter is severed or the pelvis torn and the kidney lacerated with urine escaping from the wound, results are usually poor unless nephrectomy is done. However, in the presence of a ureteropelvic tear, slight or no infection, and a not unsound kidney, no harm results from the flow of urine over tissues as long as it has a free exit.

Nephrectomy is a simpler procedure than most types of partial or repair operations and usually removes the cause of the bleeding. In that small group of cases where the condition of the patient is satisfactory and the kidney so damaged that ultimate nephrectomy will be necessary, or where there is uncontrollable bleeding from the kidney, nephrectomy is the procedure of choice. Nephrectomy takes less time than a partial operation, removes a potential field for infection, and limits future bleeding from the operative site. It also eliminates a secondary operation and the late disability and sequelæ which so frequently follow reparative procedures.

Nevertheless, in the early days after injury nephrectomy is difficult and hazardous. Most observers agree that in only rare instances is early nephrectomy indicated or advisable. Fraser,[1] in his report on war injuries in the British Expeditionary Forces, states that in many cases which formerly would have been treated

by nephrectomy, he would now rely on efficient drainage, leaving nephrectomy if necessary until a later date.

SUMMARY

Gunshot wounds of the kidney are usually secondary in importance to the injuries of the adjacent viscera. The location of the wounds and the presence of hematuria are the first indications of renal damage in most cases. Hematuria is usually present but not excessive in the majority of cases; in the early stages it tends to cease spontaneously after several days. Secondary hemorrhage into the bladder is a fairly frequent occurrence. Cystoscopy and excretory urography are of little diagnostic aid in acute injuries. The immediate question to be settled is whether operative intervention is imperative. Physical findings, wound of entry, pain, swelling, and hematuria generally determine the diagnosis and the location of the lesion.

There are three possible surgical procedures in the care of kidney wounds:

1. Drainage of the renal area, which permits inspection, evacuation of blood clots, and control of bleeding. This is the most satisfactory procedure in most cases and is attended by the lowest mortality.

2. Partial nephrectomy, renal repair, and plastic operations are not satisfactory in the cases of open wounds. Partial procedures do not remove the cause of the bleeding and are rarely justifiable.

3. Nephrectomy may be necessary in some cases of persistent hematuria or in the presence of multiple lacerations of the parenchyma. It removes a potential field for infection and limits future bleeding from the operative site. Nevertheless, it is a difficult and hazardous procedure in the early days after injury, and most observers agree that in only rare cases is it indicated or advisable.

BIBLIOGRAPHY

1. Fraser, J., and Drummond, Hamilton: A clinical and experimental study of 300 perforating wounds of the abdomen. Brit. Med. Jour., 1:321-330, (March 10) 1917.
2. Fullerton, Andrew: Gunshot wounds of the kidney and ureter as seen at the base. Brit. Jour. Surg., 5:248-288, 1917.
3. Lockwood, A. L.: Wounds of the abdomen. Brit. Med. Jour., 1:317, (March 10) 1917.
4. O'Conor, Vincent J.: Injuries of the kidney with remarks on the effects of trauma in general on urinary infection and stone formation. Illinois Med. Jour., 69:541-544, (June) 1936.

5. STRAUS, DAVID C.: Recent gunshot wounds of the kidney. Surg. Clin. of North America, 2:635-681, (June) 1922.
6. WALLACE, CUTHBERT: A study of 1200 cases of gunshot wounds of the abdomen. Brit. Jour. Surg., 4:679-743, (No. 16) 1917.
7. WALTERS, C. FERRIER; ROLLINSON, H. D.; JORDAN, A. R.; and BANKS, A. GRAY: A series of 500 emergency operations for abdominal wounds. Lancet, 192:206-213, (Feb. 10) 1917.

THE TREATMENT OF WILMS' TUMORS

ARCHIE L. DEAN, M.D.

From the Department of Urology, Memorial Hospital, New York

In the past few years a number of excellent articles have been written describing the treatment of Wilms' tumors. Study of these publications shows that there are well qualified adherents of three types of therapy: surgery, radiation, and a combination of surgery and radiation. Wilms' tumors are so rare that the majority of urologists and pediatrists see cases only occasionally but they recognize the seriousness of the condition. Since they are unable to find unanimity among those apparently most competent to treat the disease, they frequently ask, "What is the best treatment for a Wilms' tumor?" This paper is a brief attempt to clarify the problem.

Wilms' tumors are congenital, embryonal, mixed tumors which originate from the kidney anlage. Depending, as we believe, on the stage of embryonal development at which the tumors arise, their structure may vary considerably in the degree of differentiation of their component cells and in the number of different tissues represented. These structural differences probably are the principal reasons for wide variations in the natural history, clinical course and radiosensitivity of Wilms' tumors.

To illustrate how great these variations may be I present brief case histories of eight consecutive patients recently treated.

Case 1.—P. K., a female child of six months, was considered healthy until the day before admission when her parents found a mass in the right upper abdomen. Urologic examination demonstrated a tumor of the upper pole of the right kidney. Roentgen therapy was started immediately and the tumor promptly began to shrink. Seven days later a number of metastases appeared in the scalp. The infant died of widespread disease, five weeks after the growth was discovered.

Case 2.—R. L., a male child of three and one-half years, complained of abdominal pain. Six days later he voided bloody urine. Roentgen therapy was started within a week. The tumor of the right kidney responded favorably but a node appeared in the left supraclavicular fossa, from which tumor cells were aspirated. This node disappeared under irradiation but pulmonary metastases developed. Death occurred twelve weeks after the first symptom.

Case 3.—J. B., a female child of three and one-half years. Three months before admission a mass was found in the right abdomen. It disappeared after a few treatments with radiation. Two months later a recurrent growth filled the entire right abdomen but again it rapidly shrank under irradiation. Nephrectomy was performed and no extensions could be found beyond the kidney. The child died six months later with extensive intra-abdominal metastases.

Case 4.—P. N., a female child of eighteen months, appeared restless because of pain in the abdomen. Three weeks later a tumor of the left kidney was found. Roentgen therapy was given daily for a month. At the end of the first week of treatment no regression was noted but thereafter shrinking was rapid and the tumor was removed. Although pathologic examination showed no effects of radiation and much residual tumor, the child has been free from disease for four years and nine months.

Case 5.—E. L., a female child of three years, had a failing appetite and vomited. A physician found a mass in the abdomen which he thought was due to appendicitis. During six weeks of observation the tumor steadily grew. Roentgenograms revealed a tumor of the right kidney. When radiation was given without apparent effect, the kidney was removed transperitoneally. No extension of disease could be found beyond the kidney. The growth was a Wilms mixed tumor with no evidence of malignancy as metaplasia, hyperchromasia and mitotic figures were absent. The child remained well for ten months when there was nausea and vomiting. Examination showed a tumor of the single left kidney. This was irradiation with little benefit. Death occurred sixteen months after the first symptom. Searching examinations failed to show evidence of metastasis.

Case 6.—J. C., a male child of seventeen months, lost his appetite and vomited. A tumor of the right kidney was found. Thirteen roentgen treatments were given and the tumor markedly regressed but it never disappeared. Operation was not permitted. Two and one-half months later nausea and vomiting recurred and irradiation was resumed. Although treatment was interrupted twice for intercurrent infections, a computed tumor dose of 11 threshold erythemas was given in 7 months without decreasing the size of the mass. The child died 11 months after the first symptom. While the extent of the disease was great, autopsy showed that the principal mode of spread was by direct extension. This took place during the time radiation was administered daily. No effects of irradiation could be found on microscopic examination.

Case 7.—I. B., a boy of thirteen years, was admitted to a hospital after falling from a bicycle and hurting his left side. Nothing unusual was found and he was discharged in a week. Four months later he reentered the hospital because of pain and spasm in the left lower abdo-

men associated with a palpable mass in the left kidney region. Excretory urograms showed calcified areas in the left kidney and distortion of the calices. Exploratory laparotomy revealed a large mass occupying the middle and lower pole of the left kidney, perforation of the posterior parietal peritoneum and hundreds of small implants on the omentum. Microscopically the tumor was an embryonal myosarcoma, grade IV, not a classical Wilms' tumor. Irradiation was started three weeks later through eight abdominal portals. There was temporary improvement but the boy died a year later. This tumor grew locally so aggressively that at the time of the first symptom the perirenal tissues were infiltrated, the peritoneum had been penetrated and numerous intraperitoneal metastases were present. There never was evidence of metastasis through either lymphatics or blood vessels.

Case 8.—H. S., a female child of two years, had abdominal cramps and vomited. A diagnosis of pyelitis was made. Seven months later there was hematuria and her mother discovered a mass in the upper left abdomen. After taking excretory urograms her family physician changed the diagnosis to Wilms' tumor but no treatment was given for four months, when the child was passing huge blood clots. Finally, eleven months after the first symptom, a small dose of radiation was given. Some regression occurred but within two weeks the tumor grew rapidly and she entered the Memorial Hospital. Roentgenologic studies showed enlargement and deformity of the left kidney but no metastases. External radiation was given for five months with few interruptions until a computed tumor dose of 10 threshold erythemas had been delivered. There never was evidence of skin irritation. Shortly after treatment started the tumor began to shrink. No metastases ever appeared and this child, by far the most neglected of the series, is now well, four years and six months since treatment was given.

With clinical experiences such as these in which the disease seldom followed the same course and responded so differently to similar forms of treatment, we are forced to conclude that it is misleading to consider Wilms' tumors a clinical entity with a uniform mode of onset, with a natural history which follows a common pattern and which regularly responded to the same treatment. On the contrary we believe Wilms' tumors comprise a group of neoplasms related embryologically, but often so loosely that they may show great pathologic and clinical difference and variation in response to therapy.

With these points in mind a direct answer to the question, "What is the best treatment for a Wilms' tumor?" must be the admission that, as far as we know, there is no one best treatment. Realizing that many years must pass before analysis of the experiences of

many workers will finally solve the problem, and being unable to predict what the ultimate treatment will be, it seems reasonable at present to use both surgery and radiation as efficiently as possible.

Since, in practically every case, the disease is far advanced when the first symptom occurs, no time should be lost in establishing the diagnosis. Excretory urograms, therefore, should be made whenever there is the suggestion of a mass in the region of an infant's kidney. If the pelvis and the calices of both kidneys are not outlined clearly, roentgenograms should be taken after retrograde injections. One should persist in the examination until the good kidney has been clearly visualized because a bilateral incidence of between 7 and 12 per cent has been reported. It is uncertain that these figures represent bilateral genesis because at autopsy after death from widespread disease it is often impossible to prove that extension did not take place from one kidney to the other. At any rate, it is embarrassing to the physician and unfortunate for the patient when a Wilms' tumor of one kidney is treated and a similar growth develops unrecognized on the opposite side.

As soon as the primary tumor has been demonstrated every part of the body should be searched for metastases. If any are found the patient is inoperable. The scalp seems to be a favorite site for early spread. Even when the lungs appear normal at first, roentgenograms should be repeated every two to three weeks. Complete studies of the blood should be made and tests of kidney function should be performed. Occasionally these children have hypertension.

I believe that the treatment of every Wilms' tumor should begin with irradiation. This should continue as long as the tumor shrinks. Since the minimum curative dose for individual tumors is unknown, it is essential to treat each patient without interruption to full skin tolerance. It is noteworthy how frequently patients are given courses of radiotherapy consisting of a predetermined number of exposures, usually a dozen. While marked regression often occurs, the tumors always regenerate. Like many other therapeutic agents external radiation must be given Wilms' tumors until the desired effect has been accomplished. This point is not easy to recognize.

If radioresistance is demonstrated by failure of the tumor to regress after two weeks of daily irradiation, surgery should be employed without further delay. The best operation for a large tumor

seems to be a careful, gentle transperitoneal nephrectomy after first ligating the vessels of the renal pedicle. In addition to these principal vessels one often finds a number of dilated veins passing from the periphery of the tumor to adjacent perirenal tissues. It is well to cut these between double ligatures. After removal of the kidney a search should be made for extrarenal extensions, but as our case records show, they are not always discovered when present. For this reason it is wise to give postoperative radiation.

SURGICAL ASPECTS OF POLYCYSTIC KIDNEY DISEASE

GEORGE F. CAHILL, M.D., and GEORGE W. FISH, M.D.
New York City

The number and variety of surgical conditions encountered in patients with polycystic kidney disease is great. In a series of fifty-eight cases of polycystic kidney disease seen by us operative procedures were carried out in twenty-three. The ages of these patients ranged from three and one-half months to seventy-four years. The average age was forty.

The cases requiring operation may well be divided into six groups, as follows:

1. Where physical trauma to the kidney such as blows and falls or spontaneous rupture of cysts produce severe hemorrhage within or around the kidney.
2. Where infection within or around the kidney occurs.
3. Where obstruction to the flow of urine due to pressure of cysts within the kidney or upon the ureters is present.
4. Where obstruction or pain is due to calculi.
5. Where tumors and tuberculosis are producing actual destruction of the kidney.
6. Where appearance of a steadily increasing hypertension without other evidence of renal failure occurs.

The surgical procedures in these groups are more or less obvious and the indications for their employment classical. Prognosis is another matter and we feel is dependent upon certain important criteria. When polycystic kidney disease has progressed to a point where renal failure or impending renal failure is due to the disease itself, prognosis is poor and the results of most operative procedures are unsatisfactory. Where symptoms such as pain, hematuria, anuria, gastric distress, and failing renal function are due to factors not directly attributable to the disease itself, prognosis is excellent. The results of surgical intervention are promising, often even dramatic, and the end results are of long duration.

The surgical procedures carried out in this group of cases were: nephrectomy, six cases; incision and drainage of cysts, fourteen cases; incision and drainage of perinephritic abscesses, three cases.

Fig. 1 (right)

Fig. 1 (left)

Fig. 2 (right)

Fig. 2 (left)

There were two deaths following operation; one death two hours after operation, from shock, and one fifty days after operation, from bilateral renal infection.

Follow-ups of the operative cases may be summarized as follows: Seventeen patients are alive and symptom-free from one to sixteen years after operation. Two patients died from renal failure three years after operation; one patient from the same cause six years after operation, and one patient seven years after operation.

It is to be regretted that the excellent and long standing results which may be obtained by complete urologic work-ups and appropriate surgical treatment are often not offered to patients with polycystic kidney disease because too frequently these patients are considered by the profession in general as merely cases of polycystic kidney disease in the classical terminal stage.

Many of the patients in this group when first seen by us were thought to be beyond help. Surgical intervention has prolonged the lives and added to the comfort of many of them.

The accompanying photographs and brief histories show examples of five of the six groups into which cases of polycystic kidney disease requiring operation may be divided.

GROUP 1. TRAUMA AND SPONTANEOUS RUPTURE (Fig. 1).

Right.—White, female, aged twenty-four. History of painless hematuria following mild trauma to kidney region. Bilateral pyelogram showing ruptured cyst communicating with upper calix of left kidney. No operation. (Dr. Fish's case.)

Left.—White, male, aged forty. History of painless hematuria. No history of trauma. Bilateral pyelogram, showing ruptured cysts communicating with upper and lower major calices of left kidney. No operation. (Dr. Cahill's case.)

GROUP 2. INFECTION (Fig. 2).

White, female, aged twenty-seven. History of chills and fever; temperature to 105. Duration, two weeks. Palpable mass in left kidney. Blood culture positive for hemolytic streptococcus.

Left.—Intravenous pyelogram showing normal kidney shadow and pelvis on right. Large irregular kidney shadow on left with partially filled dilated irregular calices.

Right.—Bilateral pyelogram. Pus seen exuding from left ureter at time of cystoscopy. Operation in 1935, left nephrectomy. Pathologic condition, large multiple abscesses in left polycystic kidney.

The patient is living and well in 1941. Recent intravenous pyelograms show no change in size of right kidney pelvis or calices. This may be a case of unilateral polycystic disease. (Dr. Fish's case.)

Fig. 3 (right)

Fig. 3 (left)

Fig. 4 (right)

Fig. 4 (left)

GROUP 3. OBSTRUCTION (Fig. 3).

White, male, aged thirty-nine (in 1929). History of anuria for twenty-four hours..

Left.—Left kidney removed one year before in another hospital. Cystoscopy: Catheter passed to right kidney pelvis with difficulty because of obstruction in upper portion of ureter. Steady flow of cloudy urine from pelvis. Diagnosis: Cyst on surface of polycystic kidney completely obstructing ureter. Operation: Large cyst found compressing right ureter. Punctured. Other cysts punctured. Result: Patient alive and well in 1941.

Right.—Pyelogram taken in 1938, kidney function normal. (Dr. Squier's case.)

GROUP 3. OBSTRUCTION (Fig. 4).

White, female, aged twenty-one. History of increasing pain left kidney region for period of six months. Large palpable mass in left kidney region. Right kidney palpable.

Right.—Bilateral pyelogram taken in 1929: Very large polycystic kidney left. Smaller right kidney. Operation: Puncture of cysts in left kidney.

Left.—Results shown ten years after operation. Patient free of pain. Married and had three children in interim. Kidney function normal. (Dr. Squier's case.)

Fig. 5 (left)

Fig. 5 (right)

Fig. 6 (right)

Fig. 6 (left)

GROUP 4. CALCULI (Fig. 5).

White, male, age forty. History of bilateral pain in kidney region.

Right.—Bilateral ureterogram showing bilateral calculi.

Left.—Bilateral pyelogram of same. Operation refused. (Dr. Gile's case.)

GROUP 6. HYPERTENSION (Fig. 6).

White, male, aged forty-six. History of blow over left kidney region followed by gross painless hematuria.

Right.—Combined retrograde and intravenous pyelogram showing ruptured cyst communicating with upper pelvis. Also complete double ureter.

Left.—Retrograde pyelogram showing double pelvis and double ureter. There were two ureteral orifices. Hypertension was present without other evidence of renal failure. Bilateral puncture of cysts resulted in return of blood pressure to normal level where it has remained for one year. (Dr. Fish's case.)

A summary of the cases herein presented is given in Table I.

TABLE I. SUMMARY OF CASES

Total cases 58. Operative cases 23.
Ages five and one-half to seventy-four years; average age forty years.
Operative deaths, two.
Two patients died three years after operation.
One patient died six years after operation.
One patient died seven years after operation.
Seventeen patients living and symptom-free one to sixteen years after operation.

TABLE II. SURGICAL CONDITIONS ENCOUNTERED IN TWENTY-THREE OPERATIVE CASES

Injury with perirenal hematoma	1 case
Perinephritic abscess, unilateral	2 cases
Perinephritic abscess, bilateral	1 case
Hydronephrosis and partial obstruction from cysts, unilateral	4 cases
Hydronephrosis and partial obstruction from cysts, bilateral	6 cases
Hydronephrosis with complete obstruction of ureter due to pressure of cysts	1 case
Infection with destruction of kidney	3 cases
Calculi, unilateral	1 case
Tumor (hypernephroma)	1 case
Hypertension	3 cases

DISCUSSION

DR. CLARENCE R. O'CROWLEY (Newark, N. J.): To Dr. Dean's excellent remarks on Wilms' tumor, I would like to add a recent interesting case.

This was a little colored girl three years old. She was admitted to the hospital on December 12, 1940. Her chief complaint was a mass in the left upper quadrant for three weeks, associated with an anorexia at times.

Three weeks ago the mother noticed a mass in the upper left quadrant which seemed to be getting progressively larger. Periodically, the child would have loss of appetite, but no complaints.

Infancy was normal. There was no history of infectious diseases except for an occasional cold. No operations or accidents.

A well developed, well nourished three-year-old colored female was seen lying in bed and appearing in no acute distress. Results of examination were negative except for a very hard large mass in the left upper quadrant which was movable and moved with respiration, 3 centimeters below the costal margin and the anterior axillary line, and extending medially to a point 2 centimeters to the left of the midline.

Blood findings were essentially negative. Blood Wassermann negative. Urine negative. Cholesterol 184. Icterus index 7.5, undulant fever negative. Retrograde pyelograms showed profuse enlargement of the entire kidney, considerable dilatation of the pelvis, major and minor calices, but no distortion suggestive of a neoplasm.

From February 17, 1941 to March 7, 1941, a comparatively short length of time, in six treatments over a period of eighteen days and totaling 800 Roentgens to each of three areas, a total skin dose of 2400 Roentgens was given. This was one-fifth of the contemplated dose. On the last day of treatment, the tumor became impalpable.

A left nephrectomy was performed on April 10, 1941. Postoperative course was normal. Weight at the time of operation was thirty-eight and a half pounds; two weeks after operation, thirty-nine pounds. The child is still alive and doing well.

We have one child nine years after the operation who is doing well. That is not the usual rule.

DR. BENJAMIN S. BARRINGER (New York City): Was there an operation on the nine-year-old child?

DR. O'CROWLEY: Yes, radiation and operation.

I brought the original roentgenograms and pyelograms feeling they would be better to present in this case than lantern slides. Ret-

rograde and intravenous pyelograms were done before and after radiation and it is very plainly seen the diminution of the left kidney to normal has taken place and in the lower pole of the left kidney the tumor mass can be mapped out.

(Slide) Gross specimen. This adenomyxosarcoma, Wilms' tumor, has all the structures in it. This happened to be in the lower pole. It looks as if it were in the upper pole. The capsule was very dense in the upper field. This was adherent to the peritoneum, but I was able to strip it off very easily.

(Slide) Here we have characteristic spindle cells. (Slide) Here is your round-cell infiltration. (Slide) These are some of the tubular structures. They might be immature or early glomeruli. (Slide) Here we have cartilaginous and hyaline areas. (Slide) This is just showing that forty-two years ago, Wilms came out with his wonderful monograph—there are very few of them in existence, as I understand—on the mixed tumors of the kidney. Previous to that, Ribbert thought that these tumors were in three layers, comprised of all three germ layers, but Wilms decided it was nothing but ectoderm and mesoderm; and while a large part was spindle and round cells, he stated there were tubular structures, the nephrotome, and then smooth muscle, myotome, and cartilage and bony structures, the sclerotome. Of late, we have had another group of investigators saying that they all spring from renal blastema, muscle, cartilage, and metaplasia. But this is a question that is debatable and is still subject to controversy.

(Slide) Here is what Wilms really believed, that he had ectoderm, and here myotome, and muscle, and here plates of mesoderm, and bone-forming so that he felt that these were nothing more than inclusions. Then he goes through this monograph in substantiation of this hypothesis.

DR. RICHARD F. O'NEIL (Boston, Mass.): I should like to cite a case of gunshot wound of the kidney which I saw while serving with Base Hospital 6, A.E.F. It was not a battle wound, the man having been shot by an M.P. while resisting arrest.

There was a through-and-through wound of the left forearm and a wound of entrance just below the left costal margin and one of exit in the left flank. The bullet had not perforated either the abdominal or pleural cavities. He had a slight temporary hematuria.

A few days after entrance cystoscopy was performed and the ureters were catheterized in case surgery should be indicated later.

The patient made a satisfactory convalescence until about thirty days after injury when he developed a sudden profuse hemorrhage into the bladder, sufficient to cause retention. The clots were washed out. He showed moderate shock and anemia. A blood transfusion was done.

I explored the left kidney and did a nephrectomy.

There were a few small perirenal clots and the twelfth rib was splintered. The patient made a good operative recovery. On dissection of the kidney a necrosed area was found in the pelvis and one of the calices, which must have sloughed into a good sized blood vessel.

As has been stated by others, kidney wounds, as such, were uncommon, being part of multiple injuries and almost always fatal.

I did see one patient, however, who had a wound of the spine. He had a suprapubic cystotomy and had had a previous nephrectomy.

Dr. George Cahill (New York City): Surgery of polycystic renal disease falls into three categories. First (the largest), those cases having some surgical condition apart from their renal area must be evaluated to determine if their renal function is adequate for surgery and to determine the type of surgery or anesthesia. Second, those cases with polycystic renal disease but with some pathologic condition in the kidney requiring surgery, such as: motility, obstruction, calculi or tumor. Third, those cases in which the surgery to be done is because of the polycystic disease itself producing the need for surgery.

The paper presented is a discussion only of the latter two classifications.

An historical review of gunshot wounds of the kidney in the last war was aptly introduced by Dr. Scholl in his paper. It was may experience to have had four renal and one ureteral injuries in the Evacuation Hospital Zone of that war. All were from high explosive shells. Because of that they differed from those gunshot renal injuries seen in civil life. All the cases seen by me had other visceral damage besides the renal damage. When one considers that only 2,000 cases of abdominal injury reached hospitalization for classification and only 128 renal injuries were among these, there

were many more abdominal injuries sustained than that and these never reached hospitalization because of the severity of their injuries and the time consumed in evacuation. So it is surmised that the fatalities of abdominal injuries is higher than the hospital statistics.

In war surgery, as in civil surgery, the accompanying injury of other viscera is often more serious than the renal injury, and intra-abdominal exploration and repair of intestinal damage was the more pressing surgery. Often in tracing the path of missiles perforating the body it was necessary to find out the position of the injured at the time of the hit, so that the missile's route from wound of entrance to its location or exit might be estimated and then properly approached.

Dr. Scholl's paper is timely for those contemplating service in our contemplated future war.

DR. BENJAMIN S. BARRINGER (New York City): I rise to try to gather some information. The only list of Wilms' tumors, the end results, is that published by Ladd in Boston. He has gotten, as you know, an extraordinary 40 per cent or more of five-year cures. I have read and re-read his paper, and can find no clue as to why his cures be so much better than the whole world's. There must be some clue to it and I am wondering if our Boston men could give us an idea of how he handled the cases, whether he got them earlier or what, to account for these five-year cures.

DR. GEORGE FISH (New York City): I have a slide of an unusual case which I will show you. It is a case of polycystic kidney disease having a double ureter and double pelvis on the left side and a ruptured cyst communicating with the upper pelvis.

The presenting symptom was painless hematuria.

INDICATIONS FOR URETERO-ENTEROSTOMY

GEORGE GILBERT SMITH, M.D.
Brookline, Massachusetts

The indications for any therapeutic procedure must be based not only upon the results that are desired, but upon the results that have actually been achieved in similar cases. In discussing the indications for uretero-enterostomy, therefore, I shall first review the post-operative course of fifty-six individuals who have had one or both ureters transplanted to the bowel.

The operative mortality of uretero-enterostomy is a consideration of primary importance. My experiences with this operation might well be divided into two phases.

In the first phase, which included the years 1918-1931, various methods were tried. For example, in three instances both cystectomy and bilateral uretero-enterostomy were done at one operation. Coffey's technique No. 2 (bilateral transplantation with intubation of the ureters) was followed in a large proportion of cases during this period.

In the second phase, which began in 1931, I followed the principle that the simplest methods were the best. With a few exceptions, unilateral transplantation by the oblique method (Coffey No. 1) was done. In almost all, this was done extraperitoneally. Tubes were used only in a few dilated ureters.

During the period 1918-1931, twenty-three patients were operated on. One, a man of twenty-five with exstrophy, had a Coffey No. 2 in 1929 and was discharged seventeen days after operation. A woman of seventy-three with a vesicovaginal fistula following irradiation of the cervix also had a Coffey No. 2; she died eight days later. Autopsy showed a left hydronephrosis, bilateral acute ureteritis, thrombosis of the right iliac vein and vena cava inferior. Carcinoma of the cervix with invasion of bladder and rectum was found. Both ureteral anastomoses were well healed.

In twenty-one patients, uretero-enterostomy was done because of bladder cancer. In four of these, the operation was solely for the purpose of diverting the urine; all left the hospital and lived six weeks, five months, nine months, and one year respectively. In

ten, cystectomy was planned but death occurred before this procedure could be carried out.

Seven patients had their bladders removed. In three, the ureters were transplanted at the same time; two died of shock, the third lived for two and a half years. The four who had secondary cystectomies survived operation; their end results will be discussed later.

Since 1931, thirty-three patients have had one or both ureters transplanted. Twenty-four survived this operation; nine died. Among the patients with fatal outcome was one in whom cystectomy and ureteral transplantation were done at one time; this was an ill-advised operation which was not premeditated but was undertaken when, upon opening the bladder, I found that no other measure would accomplish anything of value. Even so, the patient lived for three weeks. Autopsy showed the right kidney and ureter to be in good condition; the left ureter, which had been intubed because it was dilated, had sloughed and leaked with the formation of local peritonitis. The left kidney was septic.

Two patients, operated upon according to Coffey No. 2 technique, died, both of intestinal obstruction. One patient, upon whom a successful left ureteral anastomosis had been done, died of streptococcus cellulitis following the removal of a non-functioning right kidney.

In the last twenty patients operated upon, only three died from the immediate results of uretero-enterostomy.

From a review of these statistics, it seems not unwarranted to believe that if patients are selected carefully and the ureters are transplanted one at a time, the immediate mortality should be not over 15 per cent and perhaps considerably less.

The late mortality from uretero-enterostomy is more difficult to estimate. Of the earlier group, the four undergoing cystectomies who survived died of recurrence of their cancer. The patient with exstrophy, operated upon in 1929, had his left kidney removed by another surgeon because of stone and pyelonephritis some five years later. He had married and so far as I know is still alive.

In the latter group, of the twenty-four patients that survived ureteral transplantation, nine died of cancer. One of these lived two and one-half years and died of carcinomatosis. At autopsy both kidneys appeared essentially normal; the pelves were only

very slightly dilated. Among those whose deaths was not due to cancer there was a man of sixty-four whose ureteral transplantations seemed satisfactory and whose operative recovery was uneventful. Three months after leaving the hospital his non-protein nitrogen was 62 mgm. per cent. Seven months after discharge, intravenous pyelography showed right hydronephrosis with poor function and no function on the left. He died one and one-half years after operation of acute pyelonephritis; although there was no autopsy, his doctor was unable to find any evidences of recurrence of cancer. Probably this patient should have had a nephrostomy, but his health had been good except for one attack of fever and vomiting. His death must be attributed to renal insufficiency secondary to uretero-enterostomy.

Another death attributable to renal failure occurred in a sixty-year-old man one and one-half years after cystectomy. The right kidney, which had been shut off by the bladder tumor, had been removed; the left ureter had been transplanted into the sigmoid. Although renal insufficiency was the direct cause of his death, it is not improbable that the ureter was occluded by cancer. The last time he visited the clinic a mass could be felt in the left lower quadrant; Dr. Leadbetter, who examined him, thought it was a recurrence. It would seem that he might be classified among those who died of cancer.

A third patient dying nine months after cystectomy showed at autopsy numerous metastatic foci of malignancy. His left kidney had been removed because it was functionless. The right ureter was partially occluded by a calculus impacted in the lower end. The kidney was large but not dilated; there was no gross evidence of infection. Incidentally, one other patient in this series had a ureteral stone which she passed with complete relief of pain and fever.

One patient who had cystectomy for cancer three months ago made an uneventful recovery, thanks to sulfathiazole, and appears to be in excellent health.

The ureters were put into the bowel in eleven patients because of non-malignant conditions. All of these patients lived. One, a woman with a vesicovaginal fistula, whose roentgenograms taken before operation showed a small calculus in the left kidney, developed a severe pyelonephritis in that kidney immediately after the ureter was transplanted. As she did not respond to treatment,

the left kidney was operated upon with the idea of doing a nephrostomy. When the kidney was exposed, a tumor, 2 centimeters in diameter, was found attached to the kidney just below the hilum. The tumor when incised had the typical "hasty pudding" appearance. The kidney was removed and the tumor proved to be a renal cell carcinoma "well demarcated from the kidney." The patient recovered; I doubt if she realizes how fortunate she is.

In December, 1934, Mrs. F., aged fifty-four, had her ureters transplanted because of a vesicovaginal fistula. It was noted that the left ureter was thin walled and dilated to a diameter of one-half centimeter. In July, 1938, she reported having had pain in the left renal area and fever. X-ray studies showed moderate dilatation but good function in the right kidney, several areas of increased density and no function in the left. The left kidney was removed.

In November, 1938, she had fever accompanied by right renal pain and passed no urine for twenty-four hours. When I saw her ten days later the kidney was not palpable or tender, the temperature was 97 degrees, non-protein nitrogen 29 mgm. per cent. In March, 1941, she said she felt "pretty well" and had had only occasional brief attacks of pain in the right renal area. Her blood pressure which had been 160/80 for two years at least, was 185/95; her non-protein nitrogen had risen to 50 mgm. per cent. She should have another intravenous pyelogram.

* * *

On March 31, 1938, Mrs. M. C., aged fifty-one, had a right uretero-enterostomy for vesicovaginal fistula and a left uretero-enterostomy on May 7, 1938. The pre-operative pyelograms were normal. On May 27, 1938, a pyelogram showed the right ureter moderately dilated but there was good function; the left showed no visible excretion. A non-protein nitrogen on May 20, 1938, was 45 mgm. per cent. December 9, 1938, a pyelogram showed the right ureter to have less dilatation than at the previous pyelogram in May; the left showed a questionable amount of dye after two and one-half hours. On June 28, 1939, the non-protein nitrogen was 41 mgm. per cent; on December 13, 1939, it was 37 mgm. per cent and on September 26, 1940, it was 29 mgm. per cent.

On July 9, 1940, Mrs. E. P. had a right uretero-enterostomy because of incontinence due to radiation of the cervix. She had considerable fever which was reduced by sulfathiazole. The left uretero-enterostomy was done October 11, 1940. On December 12, 1940, her non-protein nitrogen was 60 mgm. per cent. On April 2, 1941, her non-protein nitrogen was 58 mgm. per cent and at that time she had no pain or fever and the kidneys were not palpable or tender.

On January 17, 1936, Miss V. B., aged eighteen, had a right uretero-enterostomy for exstrophy of the bladder. On January 31, 1936, a

left uretero-enterostomy was done and on March 17, 1936, a cystectomy. On June 23, 1936 her non-protein nitrogen was 34 mgm. per cent; on January 1, 1937, it was 37 mgm. per cent; on May 2, 1939, it was 33 mgm. per cent; on May 17, 1940, it was 37 mgm. per cent; on January 13, 1941, it was 23 mgm. per cent. An intravenous pyelogram on April 18, 1939, showed the right ureter to be normal but the left was grossly dilated. The dye was excreted promptly on the right, slowly on the left.

On January 15, 1934, a right uretero-enterostomy was done on Mrs. M. M. because of submucous fibrosis. On May 1, 1934, the left uretero-enterostomy was done. The patient had diabetes which was improved after operation and she felt very well and experienced "great relief." In March, 1937, an intravenous pyelogram showed the right ureter to be moderately dilated and the left slightly dilated. Both pelves were visualized in ten minutes. On March 14, 1941, her non-protein nitrogen was 44 mgm. per cent.

Of the remaining four, two were children, one with exstrophy, one with epispadias upon whom an unsuccessful attempt at repair had been made. The boy with exstrophy, aged twelve, nine months after his operation showed bilateral hydronephrosis. Two years after operation intravenous pyelography showed both kidneys functioning well with no evidence of hydronephrosis or deformity on either side. Both of the children when last seen were in excellent health. One woman, sixty-one years of age, had a uretero-enterostomy in 1935 because of vesicovaginal fistula. We have been unable to trace her. Three months after the left ureter was transplanted an intravenous pyelogram showed good function and normal pelvis and calices on the left. The right kidney pelvis was dilated before the ureter was transplanted. Three months after the right uretero-enterostomy her general condition was excellent.

The fourth case, a young woman with exstrophy, was operated on in 1935. Following transplantation of the left ureter, she developed a left pyelonephritis. The ureter was exposed and the renal pelvis drained by a catheter passed up the ureter. After the catheter was removed the ureteral fistula closed promptly. Four years later she passed a stone from the right ureter; a month later pyelograms showed a moderately dilated pelvis and ureter on the right; the left showed less dilatation than the right.

From a study of these patients there emerges the sad fact that even though the ureteral anastomoses appear to be technically satisfactory and the patients to be reasonably well, more or less dilatation of at least one renal pelvis is likely to persist. Four of the patients developed stones which made nephrectomy necessary in two instances. One man who had had cystectomy for cancer died of renal insufficiency.

In considering the value of uretero-enterostomy, therefore, one

must take into account not only the operative mortality but the late mortality and morbidity as well.

Transplantation of the ureters was done in this series as follows:

Cancer of the bladder	40 cases
Cancer of the vagina	1 case
Cancer of the urethra	1 case
Vesicovaginal fistula	7 cases
Exstrophy	4 cases
Submucous fibrosis	1 case
Epispadias	1 case
Urinary incontinence	1 case
Total	56 cases

In retrospect, many of the patients operated upon for cancer of the bladder were not suitable for total cystectomy. Several had had cystotomy with excision of a tumor, which fact in itself might well be considered a contra-indication to a secondary cystectomy. A number of them had only one functioning kidney, which makes the operation of uretero-enterostomy more hazardous. In one patient a metastatic deposit was found in an iliac gland; this gland was removed but later the glands in the other side of the pelvis became involved and obstructed the only functioning kidney.

The strongest indication for transplantation of the ureters in vesical carcinoma, I believe, is the existence of widespread tumors of low-grade malignancy. These are difficult if not impossible to control by any method short of cystectomy.

Another type of bladder cancer in which uretero-enterostomy is indicated is that in which the growth is so situated upon the trigone or about the bladder neck that no other really satisfactory treatment can be instituted. Incidentally, three patients in whom cystectomy was done and in whom the urine was diverted by ureterostomy have lived for at least four and one-half, seven and eight years.

Vesicovaginal fistula can usually be cured by direct surgical attack. Cases occur, however, in which this is not feasible. In one of the patients in this series there were two fistulæ, one close beside each ureteral orifice. The other three patients had had radiation for cervical carcinoma; the bases of their bladders were sloughing, indurated and impossible to mobilize. A patient who died had had, in addition to radium treatment, three series of deep x-ray therapy. A portion of the left ureter excised at the time of transplantation showed fibrosis and chronic inflammation. The operative incision

broke open three days after operation and at the death of the patient six days after resuture of the wound it showed very little attempt at healing. Autopsy showed left perinephric suppuration and pyelonephritis. Intensive irradiation, therefore, may be considered a contra-indication to uretero-enterostomy.

Whether submucous fibrosis need ever be considered an indication for ureteral transplantation depends upon the success of the method recently described by Folsom of subtotal cystectomy. Uretero-enterostomy was very satisfactory in the one case in this series.

The clearest indication for this method of urinary diversion is exstrophy of the bladder. In the first place, children and young people seem to show greater resistance to renal infection and less tendency to develop hydronephrosis. Hugh Young's operation for the repair of exstrophy offers many technical difficulties, especially in connection with the formation of an effective sphincter, whereas the results from ureteral transplantation obtained by the Mayo Clinic, Lower, Higgins and others have been universally good.

CONCLUSIONS

The transplantation of normal ureters which drain uninfected kidneys does not constitute too great a risk. The late results, especially in older people, are not too good; in the majority of patients in this series one kidney at least showed evidences of faulty drainage. Calculi developed in four patients in this series. Several patients showed an elevated non-protein nitrogen, which is evidence of bilateral renal insufficiency.

The infection and dilatation of the upper urinary tract so commonly present in bladder cancer constitute a definite hazard and warrant transplantation to the skin rather than to the bowel.

The clearest indication for uretero-enterostomy is exstrophy of the bladder; incurable vesicovaginal fistula, unless accompanied by radiation changes and urinary infection, is also a valid reason for this operation.

CUTANEOUS URETEROSTOMY IN ACTIVE RENAL TUBERCULOSIS

FLETCHER H. COLBY, M.D.

From the Lakeville State Sanatorium, Middleboro, Massachusetts, and the Urological Service of the Massachusetts General Hospital, Boston, Massachusetts

One of the most distressing features of renal tuberculosis is persistent pain and discomfort from the infected bladder. These symptoms are extremely variable and sometimes disappear in a most dramatic manner within a few days after the removal of an infected kidney. With some patients, however, pain, frequency and dysuria persist, or return after intervals of weeks or years to torture these unfortunate sufferers. What can be done to relieve the intolerable discomfort of the bladder hopelessly diseased by tuberculosis?

Drugs and local treatments in our experience have failed to keep these patients comfortable. Complete rest in a sanatorium usually results in some measure of comfort, but I suspect that part of this is due to the fact that being subjected less to the demands of society, patients are less concerned about frequent voiding. Sympathectomy has given such uncertain results in the painful bladder of other conditions such as interstitial cystitis, that we have not offered this as a source of relief in tuberculosis. Even if sympathectomy did control pain it would not solve such problems as the small contracted bladder, incompetent ureterovesical valves, and strictures of the lower ureters or urethra. It seems as if dilatation and destruction of the upper urinary tract is encouraged by the contracted, ever active bladder, thickened and ulcerated by tuberculosis. Diversion of the urine from the bladder, therefore, seems to be a logical move.

The three usual methods of short-circuiting the bladder are nephrostomy, uretero-enterostomy and cutaneous ureterostomy. Nephrostomy, as Dr. Cabot said,[1] has the advantage of not burning one's bridges, but has the disadvantage of not effectively diverting the urine from the bladder unless the ureter is ligated. In this event it has the drawbacks of ureterostomy without its benefits. Nephrostomy in renal tuberculosis in our experience has not been satisfactory.

Transplantation of the ureter to the large bowel would be an ideal solution to this problem were it not for two objections: The mortality of the operation is appreciable and the danger of stricture formation at the anastomosis is probably considerable. The following case is an example:

A forty-one-year-old woman was admitted to the Lakeville State Sanatorium on January 28, 1936. Her general condition was critical,

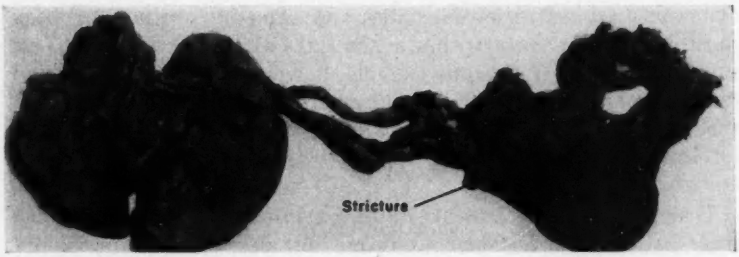


Fig. 1. Uretero-enterostomy in tuberculosis. Kidney, ureter and sigmoid two years after operation. Kidney damaged by dilatation and infection. Dilated ureter strictured at anastomosis with bowel.

with a nonprotein nitrogen of 142. She died of uremia in ten days. Five years before she had spent two years at the sanatorium at Lakeville with a tuberculosis spine and ankle. Although bladder symptoms were severe then, no tubercle bacilli were found in the urine. The bone disease became arrested but bladder symptoms were so intolerable that Dr. Quinby transplanted the right ureter to the sigmoid shortly after she left the sanatorium. It was known that there was no function from the left kidney. Except for several attacks of right-sided pyelitis she was well for over two years, voiding urine by rectum three or four times a day. Right-sided pain, a palpable kidney, uremia and death then occurred. At postmortem examination there was found an atrophic tuberculous left kidney and stenosed ureter, a dilated, septic right kidney with its ureter strictured where it entered the sigmoid (Fig. 1). It seems likely that the tuberculous ureter transplanted to the sigmoid will frequently become strictured.

Most individuals whose symptoms are severe enough to justify so radical an undertaking as side-tracking the bladder have dilated and diseased ureters. Such ureters are not best suited to anastomosis with the bowel though they are well adapted to skin ureterostomy. It has been the experience of many that the grossly diseased,

thickened or dilated ureter takes better to skin anastomosis than does the normal ureter.

Cutaneous ureterostomy has been used with success for many years in renal tuberculosis, more in Europe than in this country, I should judge from the literature. This operation has the advantage of effectively eliminating the bladder as a cause of pain and progressive renal damage. It is an irreversible procedure, however, which we suggest only when the patient understands the facts and wishes to have it done. A common objection to ureterostomy has been the difficulty of subsequent care. A great deal of this criticism, I believe, results from catheters retained in the ureters. Persistent infection and varying degrees of pyelonephritis invariably accompany their use. If urea-splitting organisms are present, as is frequently the case, stone formation is common.

Last year Dr. Keyes[2] presented a paper on this subject to show that patients with skin ureterostomies could live comfortably without catheters. Most of his patients, I believe, were those in whom tuberculosis had been present at one time but in whom the disease was no longer active. Can patients with active renal tuberculosis and with ureterostomies be spared the disadvantages of catheters in their ureters?

The problem is essentially one of stricture at the junction of skin and ureter. It seems unlikely that stricture will form in ureterostomies when there is a good rosette of ureteral mucous membrane projecting beyond the skin, any more than in well constructed colostomies. If, however, the ureter has sloughed back level with, or slightly beneath, the skin, stricture always seem to form and the stoma must be kept open by a catheter.

A technique for ureterostomy suggested in the past is simply to leave several centimeters of ureter beyond the skin at the time of operation, without any anchoring sutures whatsoever. This method has certainly resulted in the formation of an excellent rosette of pouting mucous membrane in most instances but not in all. Some ureters have sloughed back to and a little beyond the skin edges for no apparent reason such as tension, kinks, or any evident interference with blood supply. A technique which would assure a healthy projecting bud of mucous membrane would be very helpful.

Recently we have tried to accomplish this in a simple manner. The ureter is exposed through a rather high incision in the abdomi-

Fig. 2. Case 3. Tuberculosis of remaining kidney, vesicorectal fistula, skin ureterostomy. *a*, Normal appearing left kidney one month after right nephrectomy for tuberculosis. *b*, Left kidney and ureter two and a half years later dilated from progressing disease. *c*, Cystogram, vesicorectal fistula, stricture of lower ureter. *d*, Left pyelogram one month after skin ureterostomy. *e*, Left pyelogram four months after ureterostomy, no catheter in ureter.

nal wall, toward the midline rather than too near the crest of the ilium. It is carefully dissected free from the peritoneum and retroperitoneal tissue to avoid damage to its blood supply, and cleared of adhesions upward to the kidney, and downward to near the

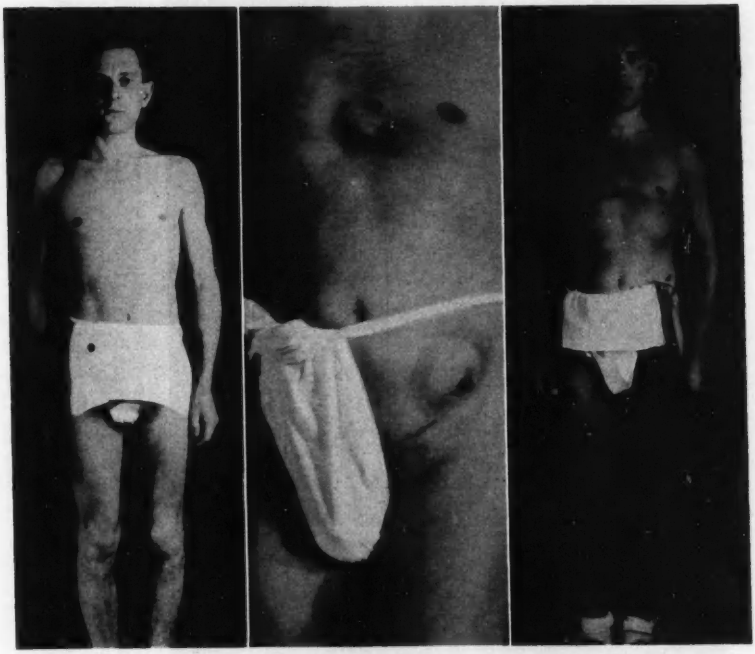


Fig. 3. *(left)* Case 3. Appearance March 22, 1940, before ureterostomy, sick, wasted and septic. Remaining left kidney diseased, vesicorectal fistula.

Fig. 4. *(center)* Case 3. Ureterostomy opening on abdominal wall (nine months post-op.). Excellent rosette of mucous membrane protruding beyond skin. A more medially placed opening is better.

Fig. 5. *(right)* Case 3. Appearance February 1, 1941, nine months after left ureterostomy. Contrast with Figure 3. Improved general condition, 40 pounds gain in weight. No catheter in ureter. The patient is kept dry and clean by a simple inexpensive colostomy bag.

bladder. The vesical end is clamped, cut and carbolized. The clamped ureter is brought out through the incision to form a gentle curve from renal pelvis to skin without tension or angulation. The wound is closed without drainage and with no soiling from infected

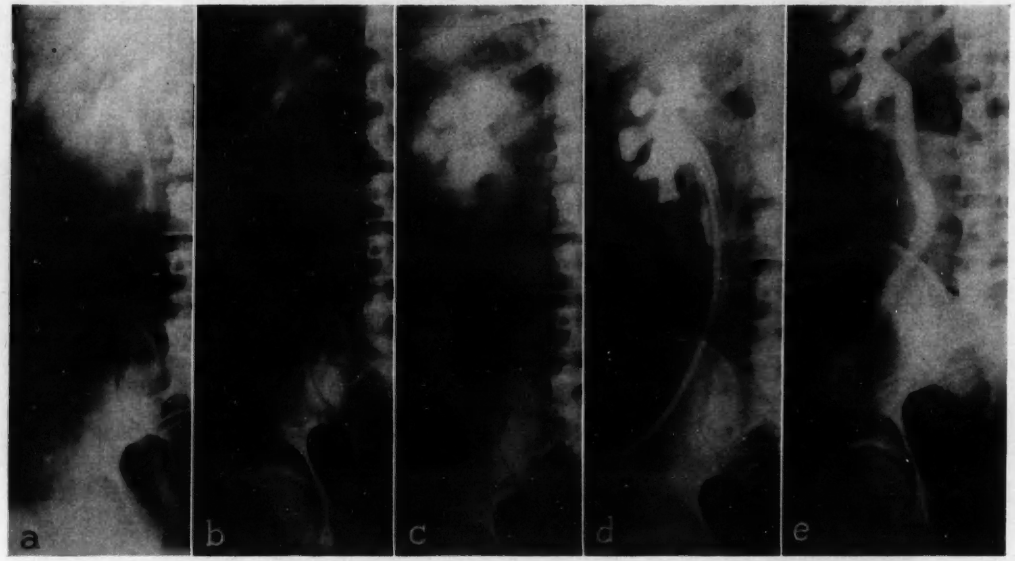


Fig. 6. Case 4. Tuberculosis of left kidney five years after right nephrectomy for tuberculosis. *a*, Left kidney not remarkable, dilatation of lower ureter. *b*, Eight months later. Beginning dilatation of remaining kidney, more dilatation of ureter. Ureterostomy suggested and refused. *c*. Two years later. Increasing renal destruction, severe bladder symptoms, non-protein nitrogen 75. *d*, Left pyelogram one month after cutaneous ureterostomy. Less renal dilatation. *e*, Left pyelogram five months after ureterostomy. Continued improvement. No catheter in ureter. Non-protein nitrogen 53.

urine. With several centimeters of ureter protruding from the closed wound the clamp is removed and a catheter passed up the ureter to the kidney pelvis. No sutures anchor the ureter to muscles or fascia since all the blood supply must be preserved. The ureter is then split on two sides along the catheter and turned down to meet the edges of the skin incision. Ureter and skin are then joined with as few silk sutures as are necessary for good approximation. The catheter is anchored to the nearby skin. In this way an accurate anastomosis of skin and ureter is encouraged without the hit-or-miss chance afforded by nature. When the wound has healed the catheter is removed and a colostomy bag is fitted to the patient. The result of this technique is shown in the illustration of Case 10 (Fig. 14). Whether such a procedure is to be uniformly successful remains to be seen.

Cutaneous ureterostomies for tuberculosis have been done on ten patients. Those who have used catheters have been distinctly less comfortable and more of a burden to themselves and others than those who have survived without catheters. The latter have succeeded in keeping themselves clean and dry and free of secondary infection and urea-splitting organisms by simple colostomy bags as suggested by Dr. Keyes. Ureterostomies without catheters may develop strictures at the skin opening, although this has not yet occurred among those who have a satisfactory rosette of mucous membrane protruding beyond the skin, even when the tuberculosis in the kidney above is active.

CASE REPORTS

Case 1. M. H., aged forty-three, had a left nephrectomy for tuberculosis in 1927. She remained well and active for eight years. Frequent urination approximated incontinence in 1935. She was admitted to Lakeville February 6, 1936, with her remaining kidney dilated, ureter tortuous, urine positive by guinea pig. Cutaneous ureterostomy was performed in May, 1936. The patient wears a catheter in the opening and changes it each week. Though there is an excellent rosette of mucous membrane outside the skin, she refuses to be weaned of her catheter. She is active and well and the urine in October, 1940, was *negative by guinea pig.*

Case 2. J. S., aged twenty-five, had bilateral renal tuberculosis complicating an infected hip and shoulder. A badly diseased left kidney was removed in 1934 with little benefit to the patient. Disease in the remaining kidney progressed rapidly. With the non-protein nitrogen at 105 a right ureterostomy was done. The patient lived about a year with

a catheter in the opening. Stones formed in the infected kidney and although he was better off with the ureterostomy he was never very comfortable and the catheter was a burden to all concerned.

Case 3. J. V. underwent a right nephrectomy for tuberculosis in

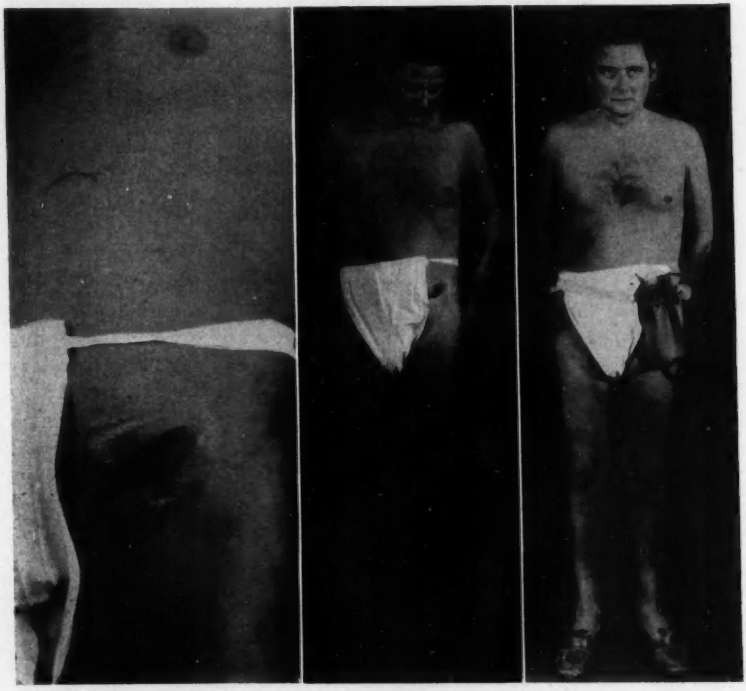


Fig. 7. *(left)* Case 4. Left ureterostomy. Junction of skin and ureter with protruding mucous membrane. No catheter used.

Fig. 8 *(center)* Case 4. General appearance of patient with skin ureterostomy.

Fig. 9 *(right)* Case 4. A colostomy bag keeps the patient dry and comfortable.

July, 1937. He was sent to Lakeville one month later with the loin wound wide open, bladder urine positive, remaining kidney normal by x-ray (Fig. 2 *a*). He was discharged from the sanatorium after a year and a half in good condition but the urine was still positive by guinea pig. He worked for seven months, then hematuria and frequency returned and urine appeared through the rectum. He returned

to the sanatorium in March, 1940, sick and septic. A large mass was present above the prostate and all his urine entered the rectum through a vesical fistula. His appearance at this time is shown in Figure 3. Some dilatation of the remaining kidney and pelvis was present (Fig.

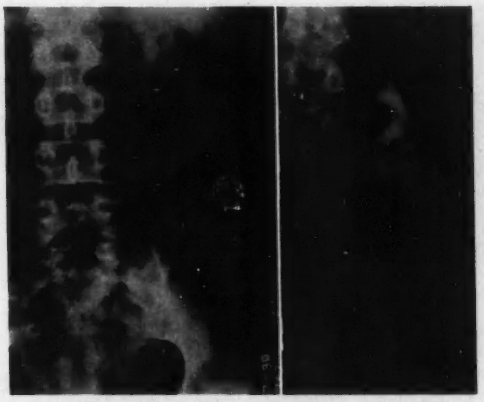


Fig. 10. Case 5. Tuberculosis of remaining kidney one month after left nephrectomy for tuberculosis. *a*, Right kidney at time of admission to Lakeville. Moderate destruction. Non-protein nitrogen 74. Severe bladder symptoms. *b*, Right kidney two and a half months after cutaneous ureterostomy. No catheter in ureter.

2 *b*) with marked stricture of the ureter by cystogram (Fig. 2 *c*). A left ureterostomy was done on April 22, 1940. The dilated ureter was histologically tuberculous. Pyelograms one month later (Fig. 2 *d*) and at discharge four months after ureterostomy (Fig. 2 *e*) show improvement. With a good rosette of mucous membrane outside the skin (Fig. 4) the patient uses no catheter, is kept dry by an inexpensive colostomy outfit, and has gained 40 pounds. Contrast his present appearance (Fig. 5) with that shown in Figure 3.

Case 4. S. H., aged thirty-four, underwent a right nephrectomy for tuberculosis in June, 1932. He continued to have trouble after operation—hematuria, urethral stricture and urinary retention. He was admitted to Lakeville in June, 1937, five years after nephrectomy. Bladder urine was positive by guinea pig, non-protein nitrogen 43, active genital tuberculosis, good renal function but dilated lower ureter (Fig. 6 *a*). Eight months later there was increased dilatation (Fig. 6 *b*), kidney urine was positive by guinea pig, there was increased frequency and non-protein nitrogen was 46. Ureterostomy was suggested and

refused. Two years later (May, 1940) there was rapid advance of disease in the remaining kidney (Fig. 6 *c*); non-protein nitrogen 75. A left ureterostomy was done July 2, 1940, and a huge thin-walled ureter brought out to the skin. Kidney function was improved (Fig. 6 *d*)

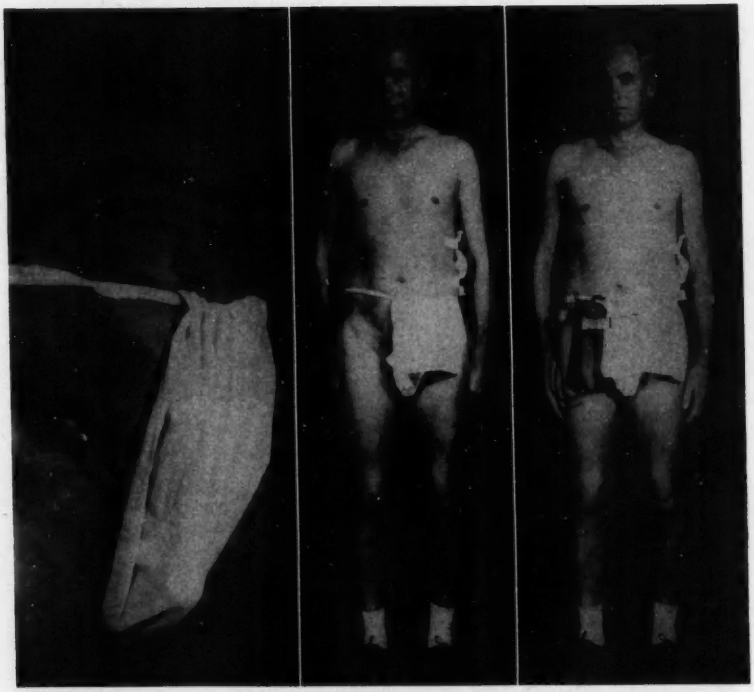


Fig. 11. *(left)* Case 5. Junction of skin and ureter. Good rosette of healthy mucous membrane outside skin.

Fig. 12. *(center)* Case 5. General appearance of patient three months after cutaneous ureterostomy.

Fig. 13. *(right)* Case 5. Colostomy bag effectively takes care of urine from the ureterostomy without a catheter.

and the catheter was removed. The patient was discharged December 18, 1940, feeding well (Fig. 8). The junction of skin and ureter was good (Fig. 7), no catheter was necessary and a colostomy bag kept him comfortable (Fig. 9). A few months ago he married.

Case 5. J. T., aged thirty-seven, underwent a left nephrectomy for

tuberculosis in April, 1939. He was admitted to the sanatorium one month later with a wide open wound, damaged and diseased remaining kidney (Fig. 10 *a*), with non-protein nitrogen 74. Nine months later non-protein nitrogen was 120. Urine was positive by guinea pig. A right ureterostomy was done in July, 1940, ureter the size of the small bowel. A retrograde pyelogram taken two and a half months after ureterostomy is shown in Figure 10 *b*. Anastomosis with skin was satisfactory (Fig. 11). General appearance was good (Fig. 12) and the patient was comfortable with a colostomy outfit (Fig. 13).

Case 6. J. S., aged thirty-three, had bilateral renal tuberculosis and was seen in December, 1939. The right kidney and ureter were dilated, and there was calcification in the left kidney without dilatation. Bladder urine was positive by guinea pig; the ureters could not be catheterized. There was increasing frequency and pain in the loins. Bilateral ureterostomy performed July 30, 1940, disclosed a dilated right ureter but small left ureter. The right ureter made a good rosette beyond the skin but the grossly normal left ureter sloughed to the skin edge. The patient was never comfortable with catheters in the ureters and died two months after operation, probably from extensive tuberculosis.

Case 7. H. O.'N., aged twenty-two, had bilateral renal tuberculosis. The right kidney became progressively worse during a year's observation in the sanatorium. It was removed in April, 1937, although the left kidney, normal by x-ray, was repeatedly positive by guinea pig. Disease in the left kidney progressed rapidly during the next one and a half years and ureterostomy was suggested but declined. Increasing pain and the formation of a vesicorectal fistula persuaded the patient to request ureterostomy eight months later. A left ureterostomy was done on August 7, 1940. Although immediately benefited by the operation the patient died in three weeks from a perforated tuberculous ulcer of the small intestine.

Case 8. M. A., aged fifty-four, had post-tuberculous renal disease and was seen in August, 1940. Nineteen years previously both kidneys were called tuberculous and the right kidney was removed. He was well and active for many years, severe bladder symptoms appearing a year and a half before returning to the Massachusetts General Hospital. He had a small contracted bladder, dilated remaining kidney and ureter, and non-protein nitrogen was 85. A purulent urine was sterile on culture and negative to three sets of guinea pigs. A left ureterostomy was done in September, 1940. Fully 3 cm. of dilated ureter which protruded loosely beyond the skin sloughed back to beneath the skin. Without a catheter in the ureter the stoma strictured firmly and the patient became sick again. He died of uremia in four months. The kidney was riddled with infection but contained no tuberculosis.

Case 9. T. S., aged twenty-eight, had bilateral renal tuberculosis, and

was seen in February, 1939. Extensive destructive lesions were found in both kidneys. In the absence of symptoms sanatorium treatment only was continued for two years. Advancing renal disease and local

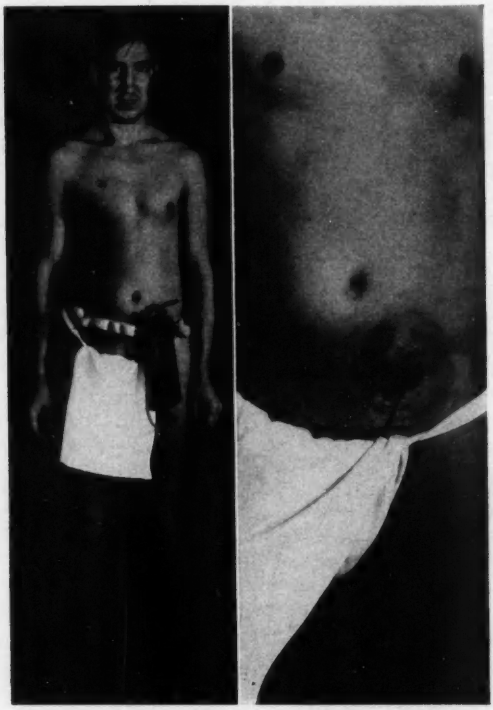


Fig. 14 *(left)* Case 10. Cutaneous ureterostomy for left renal tuberculosis. Right nephrectomy for tuberculosis two and a half years ago. Suture of inverted ureter to skin with excellent result. Good rosette of ureteral mucous membrane protrudes beyond the skin. No catheter in ureter.

Fig. 15. *(right)* Case 10. Appearance of patient two months after cutaneous ureterostomy for renal tuberculosis. Bladder symptoms relieved. Urine collected in colostomy bag without using a catheter. The patient is dry and comfortable and easily cared for.

symptoms then resulted in bilateral ureterostomy January 3, 1941. Though the ends of both ureters protruded nicely beyond the skin edges

they finally separated from the skin and catheters became necessary. The patient died, uremic, with a non-protein nitrogen of 240 a month later. Ureterostomy did not help him.

Case 10. F. K., aged twenty-five, underwent a right nephrectomy for tuberculosis in June, 1938. Frequency and hematuria persisted. He was admitted to Lakeville one year after operation. Bladder urine was positive by guinea pig. Decreased renal function and increasing dilatation of his remaining kidney occurred during the next year. A left ureterostomy was done January 4, 1941. A dilated ureter was brought out through the skin. Its end was inverted and sutured to the skin edges. The result was an excellent rosette of ureteral mucous membrane protruding beyond the skin (Fig. 14). He is comfortable, clean and active with a colostomy bag and without a catheter (Fig. 15).

CONCLUSIONS

Certain conclusions can be drawn from these ten cases of renal tuberculosis in which the ureters were transplanted to the skin. Advanced disease was present in all. In many there were genital lesions, active bone tuberculosis, and probably other areas of unsuspected disease, although there were no active pulmonary lesions. The operation of cutaneous ureterostomy entails little risk; no deaths resulted directly from the operation, although one patient died from a ruptured tuberculous ulcer of the small intestine before leaving the hospital. Simultaneous bilateral ureterostomy was done upon two patients who had tuberculosis of both kidneys. Both died within a few months and neither was particularly benefited while alive. Considerable benefit from the operation resulted in those patients whose remaining kidney was diseased after the removal of the opposite tuberculous kidney. With them intolerable bladder symptoms were relieved and the progress of renal damage was lessened. Five such patients with ureterostomies are alive and useful. If the operative result is a rosette of ureteral mucous membrane projecting beyond the skin, there is reason to believe patients can live comfortably without catheters and that they may escape stricture formation at the skin, *even in the presence of active renal tuberculosis.* If this is true these patients can easily care for themselves without the nuisance of changing catheters, and the danger of pyelonephritis, secondary infections with urea-splitting bacteria, and stone formation, is lessened. Skin ureterostomy, as usually performed, holds no guarantee of a satisfactory junction of skin and ureter. A simple method which may help to accomplish this is

suggested. Cutaneous ureterostomy is the most effective method of relieving symptoms from the hopelessly infected tuberculous bladder.

REFERENCES

1. Cabot, H., and Scherer, R. G.: Choice of methods of diverting urinary stream above level of bladder. Ann. Surg., 102:849-862, 1935.
2. Keyes, E. L.: Cutaneous ureterostomy for relief of intractable bladder tuberculosis. Jour. Urol., 44:40-46, 1940.

UNUSUAL TYPES OF OBSTRUCTION AT THE URETEROPELVIC JUNCTION

C. D. CREEVY, M.D.

From the Division of Urology, Department of Surgery, The Medical School, Minneapolis, Minnesota

Non-calculous obstruction at the ureteropelvic junction first assumed clinical importance in 1886 when Trendelenburg excised a spur between the renal pelvis and the adjacent ureter. Other conservative operations have since been devised by Küster (1892), Fenger (1894), Gayet, Young, von Lichtenberg, Schwyzer, Foley, Priestley, and others. The Y plasty of Schwyzer and Foley (Fig. 1) has the advantage of maintaining the continuity of ureter and pelvis, thus minimizing recurrent stricture, and of widening the junction without buckling, distortion, or spur formation, some of which may follow each of the other operations.

Four types of obstructing lesions are usually described: stricture, distortion by peripelvic fascia, accessory vessels to the lower pole, and neurogenic dysfunction.

Stricture is easily recognized. Its frequent occurrence in children in the absence of infection bespeaks a congenital origin.

Peripelvic fascia may squeeze the upper ureter against the pelvis, and produce a deformity which has also been called "high insertion of the ureter" and "valves at the ureteropelvic junction." The fascia is usually easily dissected off and appears to be congenital rather than inflammatory in origin.

The relationship of accessory polar vessels to obstruction is in doubt. While Quinby believes that pulsation of the artery against the junction disturbs peristalsis, veins unaccompanied by arteries may cause hydronephrosis, and neither arteries nor veins ordinarily cause obstruction unless peripelvic fascia distorts the junction about them, or a ptosis stretches it over them. It is doubtful whether accessory vessels by themselves ever cause trouble.

Neurogenic dysfunction is less tangible although von Lichtenberg has found it in 80 per cent of his cases. It is usually diagnosed when the pelvis is dilated and the ureter normal, but no anatomic obstruction can be found, and includes spasm of the junction, atony of the pelvis, and disproportion between pelvic and ureteral peristalsis.

Other types of obstruction are encountered infrequently. Ponfick and Aragona have each described a valvular flap of mucosa overhanging the junction. This is evidently different from the valve formed by the apposed pelvic and ureteral walls when the two are held together by a layer of fascia. Neoplasms of the renal parenchyma or pelvis or of the commencement of the ureter may compress the junction, but are beyond the scope of this paper.

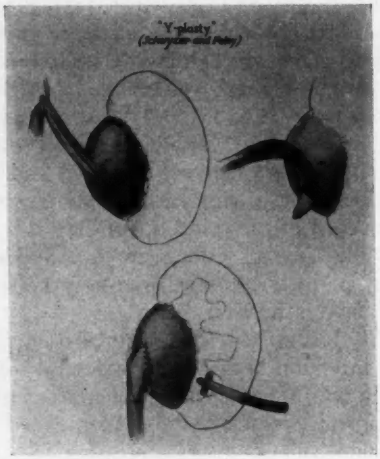


Fig. 1.

Many surgeons still employ nephrectomy rather than risk an unsuccessful plastic when the opposite kidney is normal, particularly since the indications for plastic operations are not clear cut. Infection is not a contra-indication to a conservative operation; chronic infection may be ignored, while most acute infections will respond to sulfonamides and preliminary drainage by inlying ureteral catheter or nephrostomy.

The degree of hydronephrotic atrophy which demands nephrectomy is uncertain. Since experiments indicate that one-fourth of one kidney may sustain life, it may be justifiable to conserve an organ containing as little as one-fourth of the normal amount of parenchyma. This is especially true of infants and children with great powers of repair, and in whom a normal looking opposite kidney may later become obstructed. Elderly persons with a normal

opposite kidney gain little from conservation of a crippled organ, but when the other kidney is abnormal or absent, conservatism is indicated at any age.

Certain definite rules must be followed if a plastic operation is to succeed. First is a correct diagnosis, since it is easy to attribute extrarenal pain to a borderline hydronephrosis. At operation, the kidney should be emptied before one judges the degree of atrophy, because a tense but atrophic kidney may feel almost normal. The junction must be freed of peripelvic fascia so completely that no tags remain to reproduce distortion after healing. Accessory vessels to the lower pole must be cut even though they do not compress the junction. Upward displacement of the vessels is unsatisfactory; they may later embed themselves in the pelvis itself and cause recurrent obstruction (Case 5). If the extrarenal pelvis is much dilated and flabby it should be excised, and closed with fine catgut. It is impossible to estimate future shrinkage; peristalsis in a large pelvis will be inadequate despite a wide junction, and may cause pain and infection. Nephrostomy should be made with a Malecot catheter since a plain catheter may slip out, cause extravasation, and necessitate nephrectomy. The flap should be wide to insure a good blood supply and a wide junction. Suturing, using 0000 catgut, should be accurate. Nephropexy aims merely at a straight ureter; Deming's simple and effective method is used.

I am opposed to the "ureteral splint." Having observed in hypospadias that newly constructed urethras containing catheters healed badly, while 60 per cent of those without foreign bodies healed by first intention, I am convinced that the ureteral splint merely delays healing.

The following cases of obstruction at the ureteropelvic junction represent unusual pathologic types, although the symptoms, pyelographic findings, and treatment are those of the commoner varieties.

UNUSUAL INTRINSIC LESIONS

Case 1.—R. S., aged ten, had had recurrent chills, fever, and pyuria for six years, due to an infected left hydronephrosis with a normal ureter.

At operation in November, 1932, the thickened ureteropelvic junction contained a granuloma 3 mm. in diameter in the mucosa of its posterior wall. It was excised and Y plasty done.

Six years later the patient was entirely well, the urine was clear, and the pyelogram was unchanged.

Fig. 2. Pre-operative pyelogram.

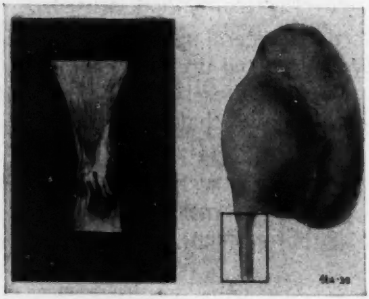


Fig. 3. Case 2. Polyps at ureteropelvic junction.

Case 2.—W. T., aged eighteen, had had intermittent left flank pain for five years from an infected left hydronephrosis with a nodular filling defect in the upper ureter (Fig. 2).

At operation in May, 1939, the thickened ureteropelvic junction contained multiple mucosal polyps (Fig. 3) of inflammatory origin. The

junction and two-thirds of the pelvis were excised and the ureter reimplanted (Küster).

Eighteen months later the patient was symptom-free, the urine was clear, and the pyelogram much improved.

Cases 3 and 4.—These cases were similar to Case 2. One, C.M., was fourteen, and the other Ch. M., was eighteen. Each had a large left hydronephrosis with a normal ureter. In both, inflammatory polyps protruded into the ureteropelvic junction from a mucosal ridge; in Case 4 the junction was also kinked by peripelvic fascia. Excision and Y plasty were done. At the last checkup examination, both patients were entirely well, had clear urine, and exhibited striking improvement on pyelography eight and eighteen months later.

Fig. 4. Pyelographic deformity from accessory renal vessel deliberately left at original operation.

COMPRESSION OF THE RENAL PELVIS BY ACCESSORY RENAL VESSELS

Case 5.—Dr. E. J. C., aged forty-two, had long had attacks of pain in the right flank with oliguria followed by polyuria. He had bilateral infected hydronephroses with normal ureters, the left kidney being a functionless sac.

At operation in May, 1937, a pair of large accessory vessels was seen to cross the right ureteropelvic junction, which was also distorted by peripelvic fascia; even after the vessels were elevated and the fascia removed, urine could not be squeezed into the ureter. Y plasty and

nephropexy left the vessels an inch above the junction; they were preserved because they were quite large and the left kidney was functionless. No relief was obtained, and pyelography a year later disclosed a normal junction with compression of the renal pelvis an inch above it (Fig. 4). Excision of the embedded vessels also failed, and the patient still wears a nephrostomy tube.

This miserable failure was unquestionably due to the preservation of the accessory vessels, and indicates that any operation which leaves such vessels in front of the pelvis carries a large risk of failure. The possibility of a stricture at the anastomosis makes me mistrust division of the junction or pelvis and re-implantation or anastomosis in front of the vessels.

COMMENTS

These five cases were selected from a series of thirty-eight operations for non-calculous obstruction at the ureteropelvic junction done at the University Hospital since 1932. In twenty-two of these, more than one cause of obstruction was found at operation, while a single cause was thought to be operative in sixteen (stricture 5, spasm 4, peripelvic fascia 4, granuloma 1, and mucosal polyps 2). Anomalous vessels to the lower pole were present in fifteen, but were not regarded as the sole cause of obstruction in any instance, since they were accompanied by fascial distortion in seven, spasm in five, and stricture in three instances.

No identical cases have been found in a fairly careful search of the literature. In the first three cases the unusual mucosal lesions were apparently the sole cause of obstruction. It seems probable that granulomata such as occurred in Case I preceded the polyps seen in Cases 2, 3, and 4, and that ulceration in the course of a pyelonephritis may have been the initial lesion in each. A congenital origin must be considered. In Case 4 the mucosal lesions were undoubtedly incidental to infection following obstruction produced by peripelvic fascia. It is included merely for completeness.

Since obstruction at the ureteropelvic junction in a given case often has more than one cause, and since it may be due to proliferative lesions of the mucosa, one should never be content to treat the condition by dividing anomalous vessels and making a nephropexy. Instead, after removing all extrinsic causes such as accessory vessels and peripelvic fascia, the junction should be opened and inspected critically. This adds nothing to the hazard of the operation (thirty-eight cases without a death) and greatly increases the chances of success. One should remember that the most favorable

time to make a successful plastic is at the first operation, since scarring from a previous operation may defeat the second one, as in Case 5.

Case 5 is cited primarily to emphasize the fact that the preservation of vessels to the lower pole, even when the operation leaves them well above the junction, is hazardous. In all other cases in which anomalous vessels were present they were divided. In no instance did serious complications ensue.

SUMMARY AND CONCLUSIONS

Non-calculous obstruction at the ureteropelvic junction is usually due to stricture, to distortion by peripelvic fascia, to kinking about accessory vessels by ptosis or peripelvic fascia, or to neurogenic dysfunction.

A plastic operation is indicated when the kidney contains enough normal tissue to sustain life. It is especially indicated in the young, and in those with bilateral lesions.

The most satisfactory operation for this condition is the Y plasty of Schwyzer and Foley.

Five examples of uncommon types of obstruction are reported, including one granuloma and three polyps of the mucosa at the junction, and one instance of obstruction of the pelvis itself by accessory vessels following Y plasty.

Four were treated by Y plasty, and one by excision of the redundant pelvis and re-implantation of the ureter.

The occurrence of polyps contra-indicates any operation which does not include careful exploration of the mucosa of the ureteropelvic junction.

When accessory vessels cross the ureteropelvic junction they should be excised even though a plastic procedure may leave them well above the junction, since they may later embed themselves in the pelvis and reproduce obstruction.

BIBLIOGRAPHY

1. Aragona, G.: Contributo allo studio della idronefrosi secondaria a valvole ureteriche congenite. Pathologica, 28:504-507, 1936.
2. Deming, C. L.: Nephroptosis: Causes, relation to other viscera, and correction by a new operation. Jour. A.M.A., 95:251-257, 1930.
3. Fenger, C.: Operation for the relief of valve formation and stricture of the ureter in hydro- or pyonephrosis. Jour. A.M.A., 22:335-343, 1894.
4. Foley, F. E. B.: New plastic operation for stricture at uretero-pelvic junction; report of twenty operations. Jour. Urol., 38:643-672, 1937.

5. GAYET, G.: Resection orthopedique du bassinet. Jour. d'urol., 1:625-632, 1912.
6. KÜSTER: Ein Fall von Resektion des Ureters. Arch. f. klin. Chir., 44:850-854, 1892.
7. PETREN, G.: A casuistic contribution to the problem of conservative operative treatment of hydronephrosis. Acta chir. Scand., 82:243-261, 1939.
8. PONFICK, E.: Ueber Hydronephrose des Menschen, auch im Kinder—und Säuglingsalter. Beitr. z. path. Anat. u. z. allg. Path., 50:1-70, 1911.
9. PRIESTLEY, J. T.: Conservative surgical treatment of non-calculous hydronephrosis. Surg., Gynec. and Obst., 68:832-841, 1939.
10. QUINBY, W. C.: Factors influencing the operative procedure in hydronephrosis. Jour. A.M.A., 93:1709-1710, 1929.
11. SCHWYZER, A.: The clinic of Dr. Arnold Schwyzer. Surg. Clin. North America, 3:1441-1475, 1923.
12. VON LICHTENBERG, A.: Hydronephrosis. Am. Jour. Surg., 7:747-756, 1929.
13. YOUNG, H. H.: Obstruction to the ureter produced by aberrant blood vessels. Surg., Gynec. and Obst., 54:26-38, 1932.

DISCUSSION

DR. BENJAMIN S. BARRINGER (New York City): Mr. Chairman, may I speak to Dr. Colby's interesting and illuminating paper on the uretero-enterostomy in tuberculosis of the bladder and kidney? If he aims at simply the control of pain and not the control of a hydro-ureter or hydronephrosis-infected kidney, I am wondering if the intraspinous injection of absolute alcohol might not accomplish what he wants to do, without the bad after-effects of the ureters in the skin. We have done that in some fifteen cases of carcinoma of the prostate and bladder with some failures and some quite extraordinary results. It certainly might have some interesting effect upon the bladder itself if you relieve the patient of the pain of urination. It is worth trying.

DR. CHARLES C. HIGGINS (Cleveland, Ohio): I agree with Dr. Colby's statement that the major complication which ensues following the performance of a cutaneous ureterostomy is a slough of the portion of the ureter which protrudes beyond the skin. Years ago, a suggestion was made by Dr. Beer, which I think is of inestimable value in preventing this complication, and that is the immediate application of warm saline dressing to the stump of the ureter for several days following the performance of the cutaneous ureterostomy.

Only a few technical points merit consideration. First, the ureter should not be stripped, as we must be certain to maintain an adequate blood supply to the ureter itself. Second, the ureter should be freed down towards the bladder as far as possible in order to avoid tension on the portion of the ureter that protrudes beyond the skin when the ureter is brought out at this site. This, of course, obviates the necessity of suturing the ureter to the skin and further impairing the blood supply. Third, after the cutaneous ureterostomy has been done, a small ureteral catheter should be passed up the pelvis of the kidney and left *in situ* for a few days, surrounding the stump of the ureter and the catheter with moist saline dressings. This prevents leakage of urine at the operative site.

There is another point which was mentioned by Dr. Smith which is also of considerable importance. I believe we see many patients in whom it is technically impossible to perform a cystectomy for

carcinoma of the bladder with a relatively low operative mortality. In many instances, however, the ureters are dilated to such an extent that it is not technically possible to transplant the ureter into the rectosigmoid without carrying a high operative mortality. In this group, as Dr. Smith mentioned, instead of transplanting the ureters into the rectosigmoid, the ureters should be transplanted into the skin, followed by complete excision of the bladder.

DR. LEON HERMAN (Philadelphia, Pa.): I would like to ask Dr. Colby how satisfactory the colostomy bag is for the purpose mentioned. Urine has the perverse tendency to escape, and I have never encountered a case in which ureterostomy was done that could be kept clean and dry by means of bags. Our patients have to wear indwelling catheters and while there are inherent dangers in this practice, some of the patients do very well indeed.

This slide illustrates widespread, diffuse, tuberculous pyelonephritis in a patient upon whom ureteronephrectomy was performed in 1934. This was followed by presacral neurectomy which served to control pain, but increasing frequency of voiding led to ureterostomy which was done in June, 1935. This individual has worn a catheter, and is quite well and entirely comfortable. It was necessary, however, to move the ostium of the ureter to the region of Petit's triangle before a satisfactory result was obtained. We usually bring the ureter onto the skin in the latter region, which may explain our dissatisfaction with the colostomy bag. Ureterostomy is a life saving measure in cases with tuberculosis in single (acquired) kidney when contraction of the vesical end of the ureter threatens the life of the organ. It is less often indicated because of extreme vesical irritability in our experience.

DR. DAVID M. DAVIS (Philadelphia, Pa.): There are lots of things I'd like to talk about, but I will confine myself to Dr. Creevy's paper, and particularly to the question of the ureteral splint. I would like to announce myself now as an unmitigated and uregenerate supporter of the splint. I think the splint not only is desirable in these operations, but also is necessary to success.

I would like particularly to attack Dr. Creevy's reasoning in regard to the presence of a splint in hypospadias operations. As a matter of fact, nobody with any sense puts a splint in a hypospadias operation, but the situation in a hypospadias operation is entirely different from the situation at the ureteropelvic juncture.

The thing we must necessarily avoid in the hypospadias operation is the production of an external fistula, and the newly constructed urethra is only a couple of millimeters from the surface, which is a very different proposition from the meter. We must get primary healing in a hypospadias. Primary healing is impossible in many uretero-pelvic operations where there is already a terrific infection present in the kidney.

I might offer another analogy of the strictured urethra. Certainly it is a very simple matter to excise a urethral stricture, together with the surrounding diseased fibrous and inflammatory tissue, place a urethral splint, and leave it there as long as you like, two weeks, three weeks, a month. When the tube-splint is removed, the urethra will be of normal character, perfectly supple and normal as far as function is concerned. This same thing, I believe, applies to the ureteropelvic juncture.

There is no particular limit to the length of time a splint can be left in. As a matter of fact, although I haven't yet enough material along this line to offer it formally, which I hope to do in the future, I am inclined to think you do not have to do anything about a stricture of the ureteropelvic juncture, except to incise the ureter longitudinally, put in a splint, and leave it there a few weeks. If this should turn out to be the case, I shall make a future publication concerning it.

DR. FLETCHER H. COLBY (Boston, Mass.): Dr. Barringer, our experience with the alcohol injection has been chiefly confined to patients with advanced malignant disease and it has seemed to me that in the first place, the alcohol injection did not satisfactorily control the pain in many instances; in other instances, we have had a certain amount of trouble from incontinence of the rectal sphincter. Actually, I don't think alcohol injection answers this problem. It does not make a large bladder out of a small, contracted, fibrous, irreparably damaged organ, which I think contributes very largely to renal damage.

Dr. Herman, I don't think there is any leak-proof colostomy bag. On the other hand, these patients I have shown have gotten along quite comfortably. They don't "stink," as Dr. Keyes said last year. They are well cared for by the simple, inexpensive colostomy bags. We buy our bags from a place in Worcester. Two bags are provided for five dollars for these patients, and they make

certain simple little improvements such as an air vent and wear them comfortably, and have said they were satisfactory.

I am perfectly convinced of this, that the patients are much more comfortable, more easily cared for, and have less tendency to infection and stone formation with colostomy bags and *without* catheters.

DR. C. D. CREEVY (Minneapolis, Minn.): I must confess that I had no occasion to bring the ureteral splint into this discussion, because it had nothing to do with the subject which I announced. (*Laughter.*) I did bring it in the hope that somebody would come out punching, because I do not believe that it is very useful.

Now, as to using a catheter as a splint in urethraplasties, my authority for doing so was Dr. Hugh Young's book. I learned for myself and from a paper by Cecil not to use it, and I think that it is up to Dr. Davis to defend himself against Dr. Young in that connection. (*Laughter.*)

I do not think that there is any analogy at all between the use of an inlying catheter to dilate an urethral stricture, and the urethral splint. In the first instance, the catheter has been used simply to dilate a fibrous stricture; in the second there is no stricture to dilate.

These five cases were culled from a series of thirty-eight operations on the ureteropelvic juncture. There have been three frank failures in those cases done sufficiently long ago to permit judging. One was a wrong diagnosis, the patient's pain being due to extrarenal disease. The anatomic result was one of the best that I have ever had, but the patient got no relief whatever.

The second was the one already discussed in which I left the vessels to the lower pole. In the third the nephrostomy tube slipped, and the resultant reaction stampeded me into doing a nephrectomy, probably unnecessarily.

Incidentally, these cases of polypoid thickening of the mucosa constitute a very powerful argument against the practice of dividing accessory vessels and making a nephropexy without seeing what the interior of the ureteropelvic juncture looks like.

Concerning Dr. Prather's statement that he would have divided the pelvis and re-implanted the ureter in a dependent portion, the last lantern slide illustrated the fact that Y plasty did in fact make

the ureteropelvic juncture dependent; the juncture, as is usually the case, was behind the vessels and not in front.

I do not believe that a better result would have followed division and anastomosis of the pelvis, but I am sure that if I had cut the vessels in the first place, the patient would have been all right. I have done that in every other instance in which I encountered accessory vessels. Only one of these patients got an infarct with a fever of 105, but he made a satisfactory recovery, and five years later had a very excellent result. I am very much in favor of dividing every accessory vessel to the lower pole, but I do want to emphasize that if there is hydronephrosis enough to justify dividing accessory vessels there is a clear indication for exploring the interior of the ureteropelvic juncture.

ENDOMETRIOMA OF THE URETER

ALEXANDER RANDALL, M.D.
From the Department of Urology, Hospital of the University of Pennsylvania Philadelphia, Pennsylvania

Whether one considers endometriomata from the histologic, the clinical or the endocrinologic viewpoint, one fact is uniquely fascinating. Medically they stand in a twilight zone; for in these neoplasms we are dealing with a histologically benign, a clinically malignant, and yet an endocrinologically responsive tumor.

One could dwell upon the embryonal theory of Von Recklinghausen, the lymph-endothelial theory of Counsellor, the metastatic theory of Halben, the ingrowth of mucosa idea of Cullen, the serosal cell theory of Iwanoff and of Meyer, or Sampson's theory of the implantation of endometrial cells through reverse, or retrograde, menstruation. To Sampson's work the weight of opinion seems to lean.

A careful review of an extensive literature has failed to reveal a reported case of intra-ureteral endometrioma, and I fear that from symptomatology and from roentgenographic visualization such growths have heretofore masqueraded as primary ureteral neoplasms. The following case of such heterotopic growth is reported to draw attention to such a possibility, for if recognition can be made, then radical surgery will be avoided.

CASE REPORT

Miss C. K., aged thirty-seven, white, was referred to the Hospital of the University of Pennsylvania November 25, 1940, by Dr. H. F. Gockley. Her complaint was right-sided pain and frequency of urination, with nocturia and hematuria. Her family history was of no importance; her past history recounted a diagnosis of poliomyelitis at six years of age, with complete recovery.

Her present illness perhaps started in 1939, about one year before our consultation, with a sense of discomfort in the right loin. In August, 1940, three months before entering the hospital, she had a moderately severe right-sided pain, associated with urinary frequency both day and night, that lasted several hours, and though it began in the loin, it radiated later to the right lower quadrant. On November 19, 1940, a severe attack, with marked hematuria, occurred, requiring more sedation than before. During the five days between this and her hospital admission the pain was present but very much lessened. There was no loss of weight; in fact, a gain of fifteen pounds during the past

year. There were no night sweats, her appetite was good and her bowels regular. Of importance is the fact that no cyclic bleeding had been observed. Menses began at fourteen years of age, after some instrumentation because of delay; they were usually regular at thirty-day intervals, and lasted five days. During the past year the menstrual interval had lessened, and twenty-one days was usual, with only three days of flow. She had always had some pain before, during and shortly after each period.

The physical examination revealed nothing abnormal, except tenderness in the right costovertebral angle and in the lower right quadrant. No mass could be felt, and only a slight, protective muscle rigidity was noticed. A urinalysis was negative, except for a few leukocytes and many red blood cells; the urine was acid. Blood urea nitrogen was 13 mgm. per cent, hemoglobin 83 per cent, and white blood cells 16,100.

An intravenous urographic study on November 26, 1940, was reported as follows:

"The survey film of the urinary tract shows no evidence of opaque calculi. The examination, after the injection of the dye, shows the urinary tract on the left side to be entirely normal in every way. On the right side there is a haziness to the shadow of the kidney pelvis, infundibula and calyces throughout. The right ureter shows multiple filling defects in the upper half, and in the lower half there is a definite, rounded filling defect around which the dye flows. The appearance is quite unusual, and I believe it is all a part of the same process. I cannot quite visualize blood or calculi producing such changes, but I would be inclined to believe that this is more likely a process involving the ureter and pelvis. Diagnosis: Generalized lesion involving the pelvis, infundibula and right ureter. Possible ureteritis cystica or multiple polyps in the right ureter."

A cystoscopic examination on November 27 showed the bladder cavity to be entirely normal in appearance. A No. 6 catheter blocked at 3 cm. when introduced into the right ureter: it was withdrawn, and crossed catheterization was successful after a slight hesitation at the same level. This catheter passed to the right renal pelvis without difficulty, and a typical, constant dripping from it suggested a mild hydronephrosis. The urine was clear and free of red blood cells.

A retrograde pyelogram was made, the report of which is as follows:

"The retrograde pyelographic study revealed the entire right upper urinary tract. There is considerable gas in the intestinal tract which tends to obscure these structures, but they are well enough seen for interpretation. The granular appearance which was evident in the intravenous study, and which was distributed throughout the kidney and ureter, is not seen in the present examination. One wonders whether this is due to an excess amount of media injected into the upper urinary tract, which would tend to blot out the fine, punctate contrast shadows seen in the intravenous study.

"Careful inspection along the border of the kidney and ureter fails to reveal any punctate defects of the character seen previously.

"At the lower end of the right ureter, about 2.5 cm. proximal to its vesical orifice, is a defect which was previously seen. The defect in the lower ureter has an appearance of a mural growth in all the films. I do not believe this is a calculus; instead, it seems definitely attached to the wall of the ureter, and could represent a benign or a neoplastic process. A ureteritis cystica is not entirely excluded, but from the retrograde pyelographic study the evidence is more in favor of a neoplasm, benign or malignant, in the distal ureter.

"Diagnosis: Mural growth of the distal end of the right ureter. Neoplasm must be excluded."

With this information, operation was performed on December 3, 1940, under spinal anesthesia. With the patient in partial left lateral position a Gibson incision was made and the retroperitoneal space entered. The ureter was identified at the crossing of the iliac vessels and appeared to be enlarged, with reduced peristalsis and having a somewhat dark color. The ureter was freed almost to the bladder. The fusiform swelling was located about 3 cm. proximal to the bladder, and on palpation the intra-ureteral contents could not be diagnosed with certainty. At this point the medial side of the ureter was found very firmly attached to the peritoneum. This tissue was stripped off the ureter without bleeding. The peritoneum was opened, and a portion of the right fallopian tube was seen and found normal. The examining finger was introduced into the peritoneal cavity, and no intra-abdominal pathology was palpated. The peritoneum was closed. The ureter was then opened above the fusiform swelling by longitudinal incision. The incision was carried over the fusiform swelling, and a cystic appearing mass, firmly attached to the ureteral wall, was discovered. The ureter was then clamped almost at its entrance into the bladder, divided and ligated. The end of the ureter was wrapped with a piece of gauze, and the ureter then freed upward as far as possible, and tucked high into the retroperitoneal space. The incision was closed with interrupted sutures of No. 1 chromic catgut, with clips for the skin. There was no drainage. The patient was then placed on her left side, and a curved right loin incision was made, muscles divided, Gerota's capsule opened, the kidney freed, and the ureter drawn upward from below. The pedicle was completely isolated, and two Herrick clamps were applied. The kidney was removed with its ureter attached. Two transfixion sutures of No. 3 chromic catgut doubled were used to ligate the renal pedicle. A single drain was left in the renal fossa, and the wound was closed with continuous sutures of No. 2 chromic catgut. Clips were again used in the skin.

An immediate examination of the removed specimen showed the kidney to be healthy, the pelvis moderately hydronephrotic, and the pelvis and ureter free of any lesions except a few punctate hemorrhages. The ureter was opened and found to be healthy until the distal end was

reached. There, on the median aspect, was a peculiar cluster of what appeared to be clear, small cysts. It did not seem to be truly papillomatous or malignant, but fulfilled the shadow of the filling defect, and it was felt that microscopy alone would give the diagnosis.

The surgical pathologist recognized in the microscopic sections some-

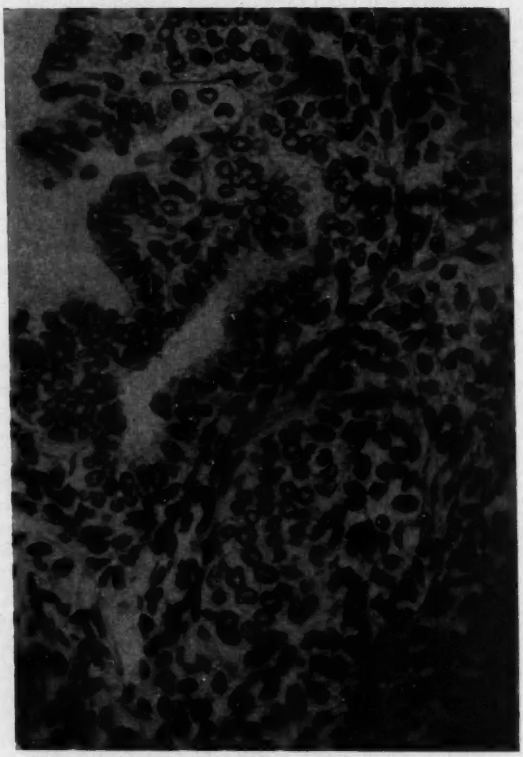


Fig. 1. High power magnification of the tissue of the intra-ureteral growth. Note typical endometrial glands and crypts, the characteristic, high, columnar epithelium with large, pale nuclei. The interstitial tissue is likewise quite characteristic of proliferating endometr'um, with syncytial cells.

thing unusual from that which was to be expected, and asked Dr. Dunne of the Department of Pathology on the gynecological service to review the slides. Dr. Dunne promptly recognized the characteristic

appearance of endometrial tissue (Fig. 1) and established the diagnosis of an endometrioma. This was further established when Dr. Dunne examined the patient postoperatively and reported that "posterior to the cervix are nodules typical of cul-de-sac endometriosis." There were no adnexal masses, but some slight induration on the right. Convalescence was uneventful.

Comment.—This case may report a great surgical rarity, but it is more likely that we have overlooked the diagnosis in some of our cases. The cyclic occurrence of intensified symptoms, especially that of hematuria, in a female in her fourth decade should always raise suspicion. Such cases should be examined for the possible presence of pelvic endometriosis, and such concomitant evidence should then warrant the delay of surgery until the diagnosis is or is not substantiated.

ENDOMETRIOSIS OF THE URINARY BLADDER

REPORT OF A CASE

WILLIAM J. BAKER, M.D., F.A.C.S.
and
JOHN I. BREWER, M.D., Ph.D.
From the Urological and Gynecological Departments of St. Luke's Hospital, Chicago, Illinois

Several theories have been postulated concerning the origin of endometriosis. The principal ones are the implantation theory, the serosal metaplasia theory, the embryonic theory (Wolffian and Mullerian tissues), the direct invasion theory, and the theory of dissemination of endometrial tissue through lymphatic and venous channels. No single theory has been universally accepted since no single theory adequately explains the development of all the widely located and variable lesions of endometriosis.

The implantation theory is based on the phenomenon of retrograde menstruation through the fallopian tubes and "spill" of endometrial fragments from the uterine cavity during gynecologic operative procedures. The bits of endometrium that are desquamated at menstruation have been shown by some workers to be viable. Others doubt their viability. It seems well established, however, that these tissues can be transplanted and can grow under suitable conditions. Multiple primary lesions may occur as a result of repeated instances of retrograde menstruation. Multiple secondary lesions may develop following primary ovarion lesions which rupture and spill fragments of endometrium into the pelvis. This type of lesion is usually the most widely disseminated and invades the abdominal viscera more extensively than multiple primary lesions. It is believed by some authors that primary residence of endometrial tissue in the ovary enhances the growth capabilities of that tissue when it becames secondarily implanted in the various pelvic structures. It is difficult at times to determine accurately whether the multiple lesions are all primary or whether they are primary in part and secondary in part.

Numerous authors deny the possibility that sloughed endometrial fragments can become implanted. In favor of this contention is the fact that implants can be produced experimentally only when fresh endometrial fragments are used. Efforts to produce growing

implants with endometrial fragments that are sloughed at menstruation have failed. Others have offered the additional criticism that this theory does not adequately explain all instances of endometriosis such as those of the umbilicus.

Advocates of the serosal metaplasia theory contend that this theory more nearly accounts for the development of all endometriosis lesions. That the serosal cells have the ability to produce endometrial gland structures is based upon observations of such changes and upon the fact that these cells are embryologically closely related to the epithelium that lines the tubes and uterus. Surgical trauma, inflammations, and hormonal stimulation have been suggested as factors that might initiate this metaplasia. Since the lesions arise *in situ* according to this theory, all must be considered primary in the peritoneum. As growth continues abdominal viscera such as the bowel and bladder walls may be involved. In the strict sense of the word such involvement of adjacent viscera must be considered as secondary to the primary lesion of the peritoneum. Thus, according to this theory, all lesions of the bladder would be secondary.

The theory of origin in embryological remnants of the Wolffian and Mullerian systems has lost favor in recent years. It is impossible to explain the origin of all lesions by this theory. The transition of the epithelium of these structures to endometrial tissue has not been conclusively demonstrated.

The direct invasion theory may satisfactorily explain such lesions as adenomyoma of the uterine wall and adenomyosis (internal endometriosis) but the origin of numerous other lesions in the pelvis cannot be accounted for by this theory.

Dissemination of endometrial fragments through lymphatic and venous channels probably accounts for some lesions. This theory, however, is not accepted with the same degree of enthusiasm as the implantation or serosal metaplasia theories. Lesions developing at some distance from the pelvis are best explained by this theory. Endometrial tissue also has been demonstrated in lymphatics. On the basis of this theory primary lesions might occur in a great many locations.

Consideration of this brief discussion concerning the etiology of endometriosis leads to two definite conclusions. The first is that the etiology is not definitely established. The second is that the terms primary or secondary endometriosis are based fundamentally upon each author's interpretation of the various etiologic possibilities and

not upon any absolute established fact. Thus the terms lose a great deal of their significance and this must remain true until the origin is unequivocally demonstrated. In view of this no attempt will be made by us to discern the primary or secondary character of the bladder lesion described in this report. Furthermore, it must be remembered that the mere presence of other lesions in the pelvis does not prove or disprove the primary or the secondary character of any bladder lesion.

Involvement of the urinary bladder wall by endometriosis is sufficiently rare to warrant the report of a single instance.

Mrs. V. M., white, aged thirty-three, was first seen by us November 27, 1939, as an office patient with the complaints of day and night frequency of urination, over a period of four years. In 1935, because of lower abdominal pain and the above symptoms, a left salpingectomy was done; all of the symptoms persisted and in 1937 a right salpingo-oöphorectomy was done. The gross and microscopic pathologic diagnoses were a hemorrhagic corpus luteum cyst 6 cms. in diameter and small follicular cysts of the right ovary. This operative procedure afforded no relief, and a hysterectomy was done in November, 1938. This pathologic report described the normal uterus which was 5.5 x 5 x 4 cms. and was amputated supracervically. The normal endometrium was as thick as 3 mm.

The patient had had four pregnancies with three normal deliveries and one spontaneous miscarriage. Her urinary symptoms had become progressively worse since the hysterectomy in 1938.

When first examined by us, her urine was normal. A bimanual examination at this time did not reveal any pelvic mass. Suspecting pathologic lesions in the bladder wall or extravesical encroachment as a result of previous pelvic operations, a cystoscopic examination was done as an office procedure on her first visit. Cystoscopy revealed a well circumscribed, intensely red lesion high up on the left posterior bladder wall. This lesion was about 2 cms. in diameter; the edges were sharp and elevated, and the base was smooth. The possibility of this lesion's being a new growth demanded biopsy and the patient was hospitalized. She entered St. Luke's Hospital November 28, 1939, on the service of Drs. Harry Culver and Wm. J. Baker and cystoscopy was repeated for biopsy purposes. The above described lesion was hard and scarred. Biopsy tissue was obtained from the edges and the base with difficulty due to the hardness of the lesion. The entire lesion and the surrounding mucosa were fulgurated. The microscopic study of the biopsy tissues revealed only chronic inflammation of the bladder wall with no invasion by epithelial tissues.

On January 3, 1940, cystoscopy was repeated because the symptoms had not improved and it was desired to discern the effect of the cysto-

scopic fulguration. The lesion had the same character as when first seen.

On February 6, 1940, the patient presented herself in the office voluntarily because of stabbing suprapubic pain in addition to frequency of urination. Direct questioning disclosed that this suprapubic pain was cyclic in character, occurring every two to three weeks. This pain was accompanied by drawing pains in the breasts. Bimanual examination revealed a tender mass approximately 3 cms. in diameter intimately associated with the bladder wall anterior to, and separate from, the cervical stump. Cystoscopy now showed a puckering of the previously fulgurated region. There was bullous edema superior and lateral to the fulgurated region. The cyclic character of the symptoms suggested endometriosis of the bladder wall. Gynecologic consultation concurred in this possibility and abdominal operation was advised.

The patient reëntered St. Luke's Hospital for the second time on March 26, 1940, on the Gynecological Service of Dr. H. O. Jones. On April 2, 1940, a laparotomy was performed by us. The sigmoid was firmly adherent to the bladder wall at a point corresponding to the location of the lesion as demonstrated at cystoscopy. The adhesions were dense and puckered at this point. No mass was discernible by inspection but the mass which had been found on bimanual examination could be palpated in the bladder wall beneath these adhesions. The sigmoidal adhesions were separated by sharp dissection and the bladder was elevated from the cervical stump. This revealed definitely that the mass was in the bladder wall. The mass and the surrounding bladder wall including the mucosa were widely resected. The bladder was closed in layers and a urethral de Pezzer catheter was placed. The remaining ovary was normal. There was no endometriosis elsewhere in the pelvis. The raw areas were peritonealized. The abdomen was closed in layers without drainage. The recovery was uneventful. The indwelling urethral catheter was removed on the tenth day. Twenty-four hours before the catheter was removed urinary antiseptics were started. In spite of this a colon bacilluria developed and persisted for three weeks. At her first voiding 300 c.c. of urine were passed and there was no residual urine. The patient was discharged from the hospital April 17, 1940. When last examined April 1, 1941, there had been no further urinary symptoms or pain, and cystoscopy showed the bladder to be normal.

Pathologic Description: The puckered piece of urinary bladder was 3 x 2.7 x 2 cms. The peritoneal side was retracted. On surfaces made by cutting there was a tought muscle and fibrous tissue, scattered through which were many small localized hemorrhagic places. Microscopic examination of this tissue revealed islets of endometrium, that included both glandular and stromal tissues extending deeply into the wall of the urinary bladder (Fig. 1). The lumens of some of the glands were markedly dilated and contained granular precipitates, red blood cells, polynuclear leukocytes, and large mononuclear phagocytes

with brown granular pigment material. Pathologic diagnosis: endometrial infiltrations of the urinary bladder wall.

DISCUSSION

This lesion of endometriosis of the urinary bladder has several features in common with most of the reported cases. The lesion was diagnosed after the patient had had previous pelvic surgery.

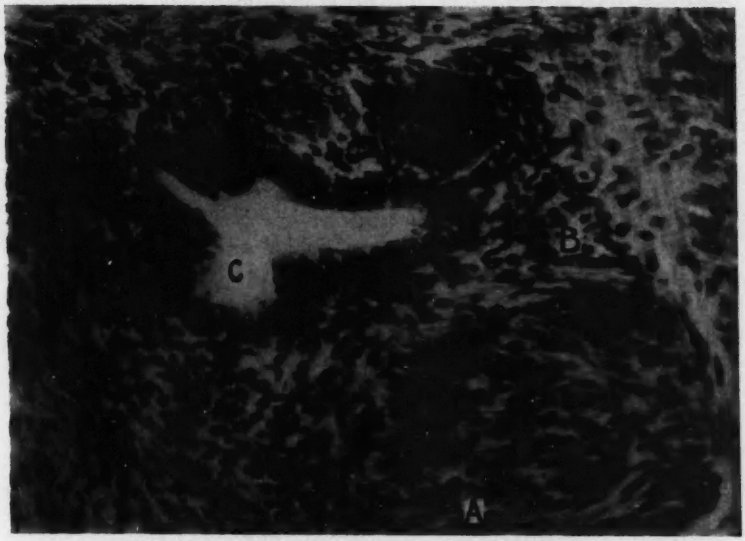


Fig. 1. Photomicrograph of endometriosis in the bladder wall. The musculature of the wall is designated by the letter *(A)*. The endometrial stroma *(B)* surrounds the endometrial gland *(C)*. No hemorrhage is shown in this particular section. Many of the other involved regions contained large amounts of extravasated blood.

The exact significance of this is not entirely clear. It has been assumed by most authors that endometriosis of the urinary bladder develops as a result of a "spill" of endometrial tissue at the time of the surgical procedure or serosal metaplasia resulting from surgical trauma or inflammation at the time of hysterectomy. That endometriosis of the bladder must, as a rule, originate in this manner is by no means an established fact. In the patient reported here, several facts suggest that this is not true. The symptoms for which

the patient was operated upon the first time, and each succeeding time, were exactly the same. Each operation, until the final one, failed to relieve the symptoms. Thus, the possibility is suggested that the endometriosis of the bladder may have been present but unrecognized previously. That the lesion did not penetrate to and produce changes in the mucosa for several years after the onset of symptoms is consistent with the report of McClelland (1938), who described a vesical endometriosis in which four years elapsed before cystoscopic examination revealed its true character. In our patient there was no endometriosis elsewhere on the peritoneum, adjacent viscera or previously surgically removed tissues.

A consideration of the diagnosis of the lesion presented here is of interest. A neoplasm was first thought of since the symptomatology of frequency of urination and suprapubic pain plus the cystoscopic findings indicated the possibility of a vesical neoplasm of an infiltrating character. The fact that this patient had had no hematuria at any time did not exclude the possibility of such a lesion since such lesions are occasionally present without blood in the urine. Multiple and adequate cystoscopic biopsies were taken from the base and edges of the lesion. These tissues revealed intact bladder mucosa and a moderate chronic inflammatory reaction of the adjacent bladder wall. No neoplastic changes were demonstrated.

Follow-up cystoscopic observation, ten weeks after fulguration of the lesion, demonstrated marked bullous edema surrounding a now puckered lesion. This reaction and the history of three previous laparotomies also suggested to us the possibility of the presence of a foreign body but did not eliminate entirely the original suspicion of a neoplasm. Endometriosis was suspected because of the cyclic character of the bladder symptoms which were associated with concomitant breast symptoms.

An adequate differential diagnosis between these three conditions was impossible. The uncertainty of diagnosis, the great probability of the presence of a foreign body, and the presence of adhesions at the site of the bladder wall lesion made it imperative that a laparotomy be done in preference to any irradiation therapy.

With the abdomen open a diagnosis was not possible. The puckered character of the adhesions suggested endometriosis but the characteristic appearance of endometriosis with peritoneal involvement could not be recognized. McClelland pointed out that there are only three cases reported in which there was no evidence of the

lesion found in the peritoneum or vesicovaginal fold. Microscopic sections in our specimen failed to demonstrate a relationship between the lesion and the peritoneum but this may have been due to the possibility that the dense adhesions in this region had distorted such relationships. There was no endometriosis elsewhere in the abdomen.

Since it was still impossible to make a positive diagnosis it was deemed wise to dissect the adhesions and resect the nodular mass and the adjacent bladder wall. When this was done and the nodule was bisected at the operating table the true character of the lesion was recognized. If a diagnosis of endometriosis could have been made without resection of the mass, a possible consideration in the treatment would have been the removal of the remaining ovary. Such removal would have undoubtedly resulted in regression of the lesion. That the urinary symptoms would have consequently been relieved is another question. The marked distortion and the fixation of the bladder may have prevented the cessation of symptoms. Another point is that removal of the only remaining ovary with the resulting precipitation of menopausal symptoms in a 33-year-old woman is not conservative surgery. A comparison of the therapeutic effects between resection of the bladder wall in the fundal region and oöphorectomy with complete castration must be considered. We believe that resection of the bladder in this particular patient was the better procedure.

If a correct diagnosis of this lesion in this patient could have been made without performing a laparotomy, a question would immediately arise as to the advisability of some type of irradiation therapy. Such irradiation would be of benefit only by using complete castration dosages. This question did not arise here because such a diagnosis could not be positively made. It is questionable whether irradiation should be used in the management of benign pelvic lesions in young women or when extensive pelvic adhesions are known to exist.

CONCLUSIONS

1. An instance of vesical endometriosis is reported in which the urinary symptoms and findings suggested three possibilities: (1) a neoplasm of the bladder wall; (2) the presence of a foreign body; (3) endometriosis.

2. The treatment of choice was surgical removal of the lesion

because of the uncertainty of diagnosis after complete examination which included cystoscopic biopsy.

3. We believe that surgery is preferable to irradiation therapy in patients with vesical endometriosis except in those near the menopause.

4. The criteria for the diagnosis of the primary character of vesical endometriosis are inadequate.

BIBLIOGRAPHY

1. Adams, P. S.: Endometriosis of bladder. Jour. Urol., 40:390-396, (September) 1938.
2. Cullen, T. S.: Adenomyoma uteri diffusum benignum. Johns Hopkins Hos. Rep., 6:133, 1896; also Adenomyoma of the round ligament. Bull. Johns Hopkins Hosp., 7:112, 1896.
3. Dannreuther, W. T.: The treatment of pelvic endometriosis. Am. Jour. Ob. and Gyn., 41:461, 1941.
4. Halban, Jr.: Metastatic hystero-adenosis. Wien. klin. Wchnschr., 37: 1705, 1924.
5. Henriksen, Erle: Primary endometriosis of the urinary bladder. Jour. A.M.A., 104:1401, 1935.
6. Ivanoff, N. S.: Adenofibromyoma cysticum sarcomatodes carcinomatosum. Monatschr. f. Geburtsh. u. Gynäk., 7:295, 1898.
7. Judd, E. S.: Adenomyoma presenting as a tumor of the bladder. S. Clin. North America, 1:1271, (Oct.) 1921.
8. Keen, F. E.: Perforating ovarian cysts (Sampson's) with invasions of the bladder wall. Report of two cases. Am. Jour. Obs. and Gyn., 10:619, 1925.
9. Keen, F. E., and Kimbrough, Jr.: Endometriosis. Obstetrics and Gynecology by Curtis, Vol. III, chap. 79, p. 339. Philadelphia: W. B. Saunders Co., 1933.
10. Kossman, R.: Origin of the glandular inclusions in the adenomyomas of the uterus and the tubes. Arch. f. Bunak., 54:359, 1897.
11. Mark, Ernest G.: Endometriosis of bladder. Jour. Urol., 37:799-807, 1937.
12. McClelland, J. C.: Endometriosis of the urinary bladder. Trans. Am. Assoc. G. U. Surg., 31:215, 1938.
13. Meyer, R.: Embryonal genesis of adenomyomas. Zentralbl. f. Gynak., 47: 577, 1923; *also* Perditoneum hyperplasia of peritoneal endothelium. Ibid., 48:722, 1924.
14. Novak, Emil: Significance of uterine mucosa in fallopian tubes with discussion of origin of aberrant endometrium. Am. Jour. Obstet. and Gynec., 12:484, 1926; *also* Pelvic endometriosis. Am. Jour. Obst. and Gynec., 22:826, 1931.
15. Perlmann, Simon: Endometriosis of the bladder. Urol. and Cutan. Rev., 38:700-703, 1934.
16. Phillips, R. B.: Endometriosis vesical. Jour. Obst. and Gynec. British Emp., 41:166-187, 1934.
17. Sampson, J. A.: Endometriosis following salpingectomy. Am. Jour. Obst. and Gynec., 16:461, 1928; *also* postsalpingectomy endometriosis. Am. Jour. Obst. and Gynec., 20:443, 1930; *also* Heterotopic or misplaced endometrial tissue. Am. Jour. Obst. and Gynec., 10:649, 1925.
18. von Recklinghausen, F.: Die Adenomyome und Cystadenomyome der Uterus und Tubenwandung. Berlin: A. Hirschwald, 1896.

19. VON SAUER, H.: Endometriosis of the urinary bladder. Zentralbl. f. Gynäk., 57:347-350, 1932.
20. WEIJTLANDT, J. A.: Endometriosis of the bladder. Proc. Roy. Soc. Med., 27:1493, 1934.
21. WHITEHOUSE, H. B.: Endometrioma invading bladder removed from patient who had never menstruated. Proc. Roy. Soc. Med., 15:1926.

ULCERS OF THE BLADDER

THE REPORT OF A CASE OF UNUSUAL ULCER OF THE BLADDER OF UNEXPLAINED ORIGIN

MONTAGUE L. BOYD, M.D.
Atlanta, Georgia

In going through the literature on ulcers of the bladder, trying to classify a bladder ulcer which I saw last year, it seemed to me that there was lacking a comprehensive survey of the subject recent enough to include the progress we have made in urology in the past twenty or thirty years. The only description I was able to find of a bladder ulcer which resembled closely the ulcer which I saw last year was in the report of a case of unusual ulcer of the bladder, by Dr. T. L. Schulte[15] from the Mayo Clinic, which was about 5 cm. in diameter, associated with a Staphylococcus aureus bladder infection, and animals innoculated with the cultured organisms tended to develop most frequently urinary tract lesions, and in one animal reproduced a similar but more extensive ulceration in the bladder. It is true that Keyes[8] in his "Urology" writes as though he were describing such an ulcer, but his reference is, as you shall see later, to Fenwick's description of an ulcer where, unless I am mistaken, the ulcer was described as incrusted which was not so in my case.

Ulcers caused by cancer, syphilis, tuberculosis, traumatic injuries, and radiotherapy need not be discussed in this paper because the diagnosis of the nature of the ulcer is fairly certain and they are generally recognized and fairly frequently seen. This presentation concerns ulcers of obscure etiology, such as those occurring with interstitial cystitis, those which have been called "simple" chronic ulcers and "simple" perforating ulcers, and ulcers of obscure "trophic" origin; also, incrusted ulcers and such ulcers as the one reported by Schulte and the one I found. Medical literature does not contain the report of many such ulcers, and in over thirty years in which I have practiced urology I have, with the exception of the ulcers of interstitial cystitis, seen only one case, the one I am reporting here. Of course, I have seen many small areas of inflammatory reaction in acute cystitis severe enough to be described as superficial ulcerations, but so far as I can see there is no connec-

tion between these and the other ulcers I shall discuss although LeFur,[10] in his monumental article on ulcers of the bladder, includes them in his discussion of bladder ulcers.

It would, for two reasons, seem to be extremely difficult to decide upon a suitable classification for bladder ulcers: (1) the rarity of these ulcers of the bladder does not afford any one man or clinic the opportunity to collect enough data for an adequate study; (2) the difficulty of determining, from the descriptions in the literature, whether or not many of the ulcers reported belong to the same class even though at cystoscopy they present different appearances. Some of the case histories reported are inadequate, while in others there is no report of the microscopic and bacteriologic examinations of the urine, and in many there is no report of the microscopic pathology. Of course, many of the ulcers were treated and cured by methods less radical than excision so that a microscopic examination was not possible.

Irrespective of etiology one might say that generally speaking ulcers can be divided into two groups, those associated with active infections and those which are not. The simple ulcer, the perforating ulcer, and the ulcer of interstitial cystitis may be and frequently are found with little or no associated changes in the urine. Infection is pronounced with incrusted ulcers and also in the third stage ulcers described by Fenwick.[5] Schulte thought that the Staphylococcus aureus infection was an important etiologic factor in his case, and I wonder whether or not the infection was the essential etiologic factor in my case.

Fenwick,[5] in 1896, described various stages of what he called simple solitary ulcer of the bladder, the *first stage* being the "simple, solitary ulcer"; in the *second stage*, the effects of bladder infection appear and the ulcer becomes incrusted; and in the *third stage*, the bladder wall becomes extensively involved and "the bladder is merely an unelastic bag holding an ounce or so." His article seems intended to give the idea that there is one etiologic factor for these ulcers and the difference in their appearance is due largely to their age, activity, and concurrent or intercurrent infection of the bladder. Walker,[16] as well as other authors, accepted Fenwick's belief that the various ulcers were stages of the simple solitary ulcer, and after due consideration his conclusions seem to me worthy of special attention.

Classification and nomenclature of the ulcers are not uniform;

encrusted ulcers have been described by some authors as though they were a separate group, and the term solitary ulcer has been employed to describe a condition which is evidently the same condition which has been called a simple ulcer by other authors, and simple, solitary ulcer by Fenwick. Cabot[3] employs the terms simple, chronic ulcer, and perforating ulcer. Buerger[1] uses the term callous ulcer to describe a somewhat advanced stage of simple solitary ulcer.

It is doubtful whether incrustation cystitis can ever be considered to be the same as incrusted ulcers of the bladder. The incrustations, no doubt, are due in both instances to the type of infection of the bladder which is present, but in incrustation cystitis the incrusted lesions seem more superficial and usually the area of bladder mucosa involved in the superficial ulceration is more extensive. Whether the injury to the mucosa of the bladder which occurs in the severe grades of cystitis due to pyogenic organisms can be accentuated at certain localized areas sufficiently to destroy the mucosa and cause the development of superficial or deep ulcers does not, as far as I have found, seem to have been definitely determined, but it would, on first thought, seem that it could happen. For in severe cystitis, it is not uncommon to observe patches of adherent mucus with quite marked changes in the mucosa, and bleeding when the adherent mucous covering is washed or pushed off. LeFur discusses ulcerations in acute and chronic cystitis and mentions cases which have been reported as ulcers. On the other hand it is hard to believe from my own experience that any of the commonly encountered pyogenic infections of the bladder can produce true ulcerations because we so frequently see severe and prolonged bladder infections with such a great variety of bacteria, which cause severe inflammatory changes in the mucosa without ever producing anything except a superficial ulceration which heals readily as the cystitis is controlled. Even in patients where the mucosa has been subjected to long continued trauma from stone, accompanied by various kinds and degrees of infection, I have never seen an ulcer, although cases have been reported (LeFur).

Some of the incrusted ulcers have only a superficial incrustation over the well developed bladder ulcer. In other instances the deposit of urinary salts extends deeply into the inflammatory changes which exist in the submucosa. From what I can learn it appears that there still may be some doubt as to whether these incrusted ulcers are a separate kind of ulcer or, as Fenwick stated, are a stage

in the development of bladder ulcers, the first stage of which is the simple solitary ulcer.

Other than the ulcers due to malignant growth, syphilis, tuberculosis, and trauma, there are two which seem to have such distinct characteristics that they can be generally recognized by the history and by cystoscopic examination—the ulcer of interstitial cystitis (Hunner's or elusive ulcer) and the simple chronic ulcer (the first stage of the ulcer described by Fenwick). The recognition of a perforating ulcer seemingly depends almost altogether upon the cystoscopic findings in the case of a spontaneous bladder rupture or finding the ulcer at a postmortem examination. The Hunner's ulcer, or elusive ulcer, which is now most commonly called interstitial cystitis, is reported to be characterized by the lack of bladder infection and of changes in the urine, the small area of mucous membrane which is visibly involved as compared to the extent of the submucous change, the cracking or splitting of the mucous membrane over and about the ulcer on overdistention of the bladder, and their chronicity and the severe disability which they cause.

The simple chronic ulcer is usually a single ulcer and it is frequently recorded that they resemble very closely in appearance the ulcers of the stomach. They are usually 1 or 2 cm. in diameter situated partly on the outer part of the trigone or near the trigonal region, and have a punched-out appearance with rather sharply defined edges, and a base which may be grey or red. It would seem that the ulceration involved essentially the mucosa and submucosa. Intermittent hematuria may vary in severity, but, as with ulcers of interstitial cystitis, the urine in the earlier stages usually shows little or no evidence of infection. Unlike interstitial cystitis the bladder symptoms are at times, it would seem from the reports of some of the cases, not at all marked until the ulceration has been present for some time or until infection of the bladder becomes active. However, Fenwick reported that pain in and sensitiveness of the penis were always pronounced symptoms in the males in the early stage of the ulcers.

The simple perforating ulcer, I infer from what I find in the literature, is almost exactly like the simple chronic ulcer except that it penetrates the bladder wall more deeply and eventually reaches the stage of perforation. For that reason it has been assumed that its destructive activity is greater so that the muscularis is involved to such a degree that perforation of the bladder wall is possible, and

in some of the reported cases it seems evident that the process had produced deeper inflammatory changes and deeper ulcerations than described in the simple solitary ulcers. With these ulcers, as with interstitial cystitis and simple chronic ulcers, infection of the bladder is not an important factor in their etiology or activity.

The microscopic pathology of simple ulcer and the ulcer of interstitial cystitis suggests the possibility of their being more or less the same process, the simple chronic ulcer being the early lesion and the ulcer of interstitial cystitis the more advanced lesion where, active bladder infection being absent, the mucosa succeeds in varying degrees in growing over the chronic inflammation which persists in the submucosa. The only thing which seems to be definitely against this is that the simple ulcer is reported as appearing nearly always partially on and about the trigone while most of the ulcers of interstitial cystitis do not involve the trigone and are for the most part not immediately about the trigone.

The perforating ulcer may, in some cases at least, be a simple chronic ulcer which ruptured before its existence became suspected or recognized, because of the fact that it was unusually extensive or unusually active or because it existed in a bladder with abnormally thin walls (which I am sure you have all seen in operations on the bladder). If a simple ulcer were present in a bladder wall which was quite thin and the bladder happened to be subjected to overdistention, or to unusual pressure while it was normally distended with urine, rupture might very well result.

I have not been able to determine that anyone has found enough difference in the underlying pathologic condition in the simple ulcer and the perforating ulcer to make an evident distinction further than that one perforates and the other does not, and George Walker[16] says this in his article on simple ulcer of the baldder, "It may be defined as a single, non-inflammatory ulcer located in the mucous membrane of the bladder, which occasionally penetrates the entire wall."

If a simple chronic ulcer neither healed nor became an ulcer of interstitial cystitis, it might very well with an appropriate intercurrent urinary infection become an incrusted ulcer, as believed by Fenwick, or with another kind of bacteria present, it might become such an ulcer as has been described by Schulte or perhaps the one seen by me. Keyes[8] says, "The solitary ulcer, as described by Fenwick, is doubtless but a large chronic elusive ulcer. The ulcer affects

the same regions of the bladder and overlies an interstitial cystitis of far greater extent than the ulcer itself. But the cystoscopic picture is quite different. The ulcer is large; in fact, I have excised one that was 5 cm. in diameter, fixed, obvious. It is a red velvety granulating surface, surrounded by an indurated border, and set in a chronically inflamed bladder. The urine is constantly purulent and contains staphylococci. There is often an associated pyelonephritis, though this is rare with the elusive ulcer. Yet the symptoms of the solitary ulcer are not, could not be, more severe than those of the elusive ulcer." And this description of Keyes fits Schulte's ulcer and the one I saw except for the indurated border which Schulte does not mention and which was not present in my case and for the fact that my patient had no urinary symptoms before the bladder infection was found.

If ulcers produced by known trauma are excluded, as I intend that they should be, from this group, we would seem to have little definite knowledge about the etiology of most of these ulcers. Trophic changes, metastatic infections of the mucosa or submucosa, the obliteration of some of the small blood vessels of the mucosa by various processes are all theories which have been advanced. LeFur and others have produced ulcers experimentally in animals but it does not seem to me that we can be sure that the conditions which they produced are the same as those we find in patients. However, the existence of some such process as blood vessel injury or obstruction, trophic changes or metastatic infection, would appear necessary for the production of ulcers which are found where little or no bladder infection exists and where there is no history of active infection having preceded the appearance of the ulcer. Walker expressed this opinion saying that the simple ulcers are "probably caused by a local disturbance in, or complete blocking of, the terminal arteries or by an interference with the trophic nerves." One of the queer things, as Fenwick pointed out, is the occurrence of some of the ulcers in young men about twenty who have no history of having had venereal disease and who are at an age where trophic and blood vessel changes would not seem likely to occur.

CASE REPORT

L. S., male, aged twenty, single, student, Piedmont Hospital No. 58731, was admitted July 1, 1940. On admission he complained of frequency of urination, hematuria, pain and burning of one year's

duration. Otherwise, he was well except that he was quite nervous and irritable and had lost 15 pounds in twelve to eighteen months.

Eighteen months before I saw him (January, 1939) he had had a urological examination by Dr. Perry Bromberg, of Nashville, Tennessee, who had made a diagnosis of bilateral hydronephrosis, probably due to anomalous vessels at the ureteropelvic juncture.

About six months later (June 15, 1939) he was admitted to the Brady Urological Institute and discharged about two and a half months after that (September 17, 1939). He was seen by Dr. Hugh Young during that time (August 17, 1939) who furnished me with complete notes of the treatment that the patient received at his clinic. After returning home in September he was treated by Dr. William Farber, a former associate of mine, under whose care he received autogenous vaccines, mandelic acid, massage, and urethral instrumentation with sounds without much benefit.

At about twelve years of age the patient had a rather severe acne over his face and shoulders and had a good deal of x-ray treatment for it, also about eight injections of antuitrin S. and autogenous vaccines.

At about fifteen (five years before I saw him) he began losing weight, albumin was found in the urine, and he became easily fatigued. During the next few years this general malaise continued and in September, 1938, almost two years before admission, his blood pressure was found to be 140, and there was a good deal of albumin in the urine. The attending physician advised that this was of no especial significance and that it be disregarded. A few months later he reported to his school physician in Cincinnati that he was having headaches, loss of weight, nervousness, trembling, et cetera. The blood pressure was then 140 to 145 and there was albumin in the day urine and none in the night urine. He was advised to quit school for a while which he did. Repeated tests of the urine during the rest period showed albumin to be absent in the early morning urine but present most of the time during the day.

In January, 1939, an intravenous urogram showed a well marked dilatation of the pelvis of each kidney but only a little enlargement of the minor calyces and of the ureters.

He then went to the Vanderbilt University Hospital where Dr. Albert Weinstein reported that a general physical examination showed nothing abnormal and that the urine and blood pressure were normal. Dr. Bromberg then made a retrograde urogram and confirmed the findings of double hydronephrosis and expressed the opinion that the ureteropelvic obstruction on the left was caused by a blood vessel (Fig. 1). He found a few pus cells in the bladder urine, but no report of the infection is to be found in the hospital record, and Dr. Bromberg made note of the fact that the bladder and ureteral orifices were normal.

On June 15, 1939, the patient went to the Brady Urological Clinic where on admission, he complained of pain in the leg and in the left

scapula and of albumin in the urine. A thorough general physical examination at the Brady Clinic showed no trouble except a blood pressure of 142/70 to 150/60 and a three plus albuminuria. The urologic examination disclosed a normal total phthalein output. Guinea pig inoculation for urinary tuberculosis was negative. The bladder urine cultures showed Streptococcus fæcalis and staphylococcus. Cystoscopy and a urogram on admission were reported to show a normal bladder

Fig. 1. Retrograde urogram January 21, 1939, by Dr. Bromberg. Bilateral hydronephrosis with a ureteropelvic obstruction on the left. The ureters and bladder show no abnormality.

Fig. 2. Intravenous urogram March 9, 1940, showing the dilatation of the ureters.

with normal ureteral orifices. There was no growth in the cultures of the kidney urine. Differential phthalein for fifteen minutes, right 20 per cent, left 15 per cent. The roentgenograms showed large extrarenal pelves with some ureteropelvic obstruction on the left and some dilatation of the ureters.

Following the cystoscopy and urogram the urine became grossly bloody and the active bleeding continued for ten days and some bleeding for about thirty days. He was examined cystoscopically on August 17 by Dr. Young, who removed a clot from the bladder and reported

that the bladder capacity was apparently small. The vesical orifice was normal. Bleeding into the bladder made visualization of the ureteral orifice and ridge region difficult, and this difficulty was increased by the discomfort produced by even a small amount of irrigating fluid in spite of the fact that the patient had spinal anesthesia. He noted that "back of the trigone the bladder is irregular, probably thrown into folds, with adherent bits of blood or possibly areas of hemorrhage into the mucosa. Certain areas along the anterior and lateral walls look like interstitial cystitis and some of these are bleeding. Back of the left corner of the trigone and bladder wall is particularly irregular. No definite ulceration, no definite tumor seen, but owing to the presence of the bleeding and the small size of the bladder, and the fact that it is thrown into irregular contractions, it is difficult to make a definite statement as to the bladder pathology."

Intermittent attacks of urgent and frequent urination accompanied the bleeding which followed the first cystoscopy. The blood clotting time was found to be ten minutes and he was then treated with vitamins, including K, and in four days of treatment the clotting time became normal and the bleeding stopped.

On discharge from the Brady Clinic, September 4, the bladder disturbances which followed cystoscopy had largely disappeared and the patient was much better—voiding every two hours by day and every three hours by night, but the urine was still infected with staphylococcus and Streptococcus fæcalis.

In October, 1939, a month after leaving the clinic, Dr. Farber made an intravenous urogram which showed not only the double hydronephrosis but also a good deal of dilatation of the lower ureters (Fig. 2) the ureteral shadows being about one centimeter wide. In March, 1940, the same condition was shown by a repetition of the intravenous urogram (Fig. 2).

When the patient came to me July 1, 1940, he was voiding about every hour to hour and a half day and night. There was urgency, and discomfort after voiding. The urine was faintly bloody, slightly acid, cloudy, and contained staphylococcus and Streptococcus fæcalis on culture. There was a moderate amount of pus and a half of one plus albumin. Blood pressure was 150/80. Phthalein test (voided): 35 per cent in thirty minutes after an intravenous injection. A general physical examination showed no pathologic lesions.

There was a good deal of pus in the prostatic secretion and the bladder above the prostate was very sensitive to pressure. The size, shape, and consistency of the prostate and seminal vesicles were normal. There was no urethral stricture and the blood Wassermann test was again negative.

Urethroscopy and cystoscopy under general anesthesia showed a normal urethra and bladder neck except for a slight elevation of the vesical orifice above the trigone and floor of the urethra.

There was a fairly good deal of bleeding from the posterior blad-

der wall where it infolds over the ureteral ridge region when the bladder is empty. With a diminution in the bleeding an ulcerated area, about 5 cm. in diameter, was seen situated on the central portion of the posterior bladder wall; it was slightly elevated above the surrounding mucosa, which looked only a little reddened. The surface of the ulcer was bright red and rough suggesting the existence of short fine villi, but perhaps best described as shaggy. The margins were only

Fig. 3. Retrograde urogram July 4, 1940. Roentgenogram made ten minutes after the catheters were withdrawn for the semi-erect roentgenogram. Retention of skiodan in the left kidney and in the lower left ureter.

Fig. 4. Cystogram with air injected into the rectum. A quite definite filling defect on the posterior wall of the bladder. One catheter in the urethra; the one to the right in the rectum.

fairly sharply defined. There was no incrustation and no visible evidence of healing at the edges of the ulcer. The ulceration and the bladder wall on each side protruded quite a good deal so as to overhang the ureteral ridge region. The ureteral ridges were not to be seen. The ureteral orifices were quite round, somewhat enlarged, the lips were thin, and the orifices were open showing the ureteral walls immediately beyond the orifices; they were situated at the place where the bladder wall turned up towards the overhanging ulcerated area.

Several coarse folds of the mucosa led to the area of the ulcer from either side and the whole protruding area seemed fixed. This fixation was discovered when I started to catheterize the ureters and found that the beak of the convex cystoscope pushed against the area so that there was a little difficulty in reaching the orifices with the catheters.

A 6 F. catheter passed up each ureter to the kidney, but some manipulation was necessary to pass through the lower ends of the ureters. There was no infection of either kidney. The intravenous phthalein test collected twenty minutes showed a 23 per cent leakage into the bladder with 9 per cent on the right and 3 per cent on the left. Twenty cubic centimeters of skiodan were injected into each kidney without symptoms. The large extrarenal pelves were found with enlargement of the ureters and a retention of skiodan for ten minutes in the left kidney pelvis and in the lower part of the left ureter (Fig. 3).

On July 8, 1940, after 4 per cent cocaine was put into the bladder, about 225 c.c. of skiodan were injected into the bladder; a cystogram then made (Fig. 4) showed an infolding of the posterior wall of the bladder. There was no extension of the skiodan into the ureters.

Treatment with sulfathiazole failed to clear up the bladder infection although the bleeding stopped and the patient's bladder symptoms were a good deal relieved.

At suprapubic operation August 29, 1940, the condition seen at cystoscopy was found. Intraperitoneal exploration showed no pathologic change about the bladder and no induration of the bladder wall could be palpated, but extraperitoneally the perivesical tissues were quite adherent and the upper and posterior parts of the bladder were freed with some difficulty. Within the bladder the area of ulceration and that part of the bladder immediately about the ulceration were seen to be slightly elevated above the surrounding surface due, it appeared to me at the time, to the fact that the bladder wall was thickened. There was no induration of the bladder wall but before the excision of the ulcerated area the wall beneath the ulcer was about 1.25 cm. thick. The ulcer measured approximately 4 by 5 cm. in diameter. With the bladder open and empty, after the upper and posterior portion had been freed, the protrusion or infolding of the area of ulceration which was seen at cystoscopy was not so evident as at cystoscopy.

The excision of the bladder wall was carried almost to the trigone and almost to the ureteral ridges on each side. The excised tissue was described by the pathologist (Dr. W. B. Matthews) as follows. "This is a fresh piece of tissue taken from the urinary bladder. It measures 7.5 by 3.5 by 1 cm. It is part of the entire wall thickness. The lining is covered by a smooth red material that looks like fibrin. Palpation of specimen indicates it is uniformly soft and pliable. Sectioning of wall shows it to be irregularly discolored. The wall is definitely hypertrophied and edematous.

"Microscopic diagnosis: Three sections were made (one frozen, two paraffin) and in all the features are similar.

"Beginning the examination on the inside of the bladder (Fig. 5), one finds absolutely no epithelium present. The lining of the bladder over this specimen is fibrous tissue with some young cells and blood vessels. Here and there are small shreds of necrotic material. There is a tremendous edema of the subepithelial fibrous tissue (Fig. 6), as

well as a great deal of extravasated blood. The latter is fresh blood, with no old pigment, and may have bled into the wall during the operation. The rest of the wall is smooth muscle and fibrous tissue. The edema mentioned above extends throughout the bladder, separating the muscle bundles. No doubt this is in large part responsible for the

Fig. 5. The chronically inflamed granular surface of the ulcer without epithelium. There is extensive new blood vessel formation, the vessels are quite full of blood, and the blood is not only in the vessels but in the tissue as well. The dark area below in the center is an actual hemorrhage into the tissue. There are some young fibrous tissue cells.

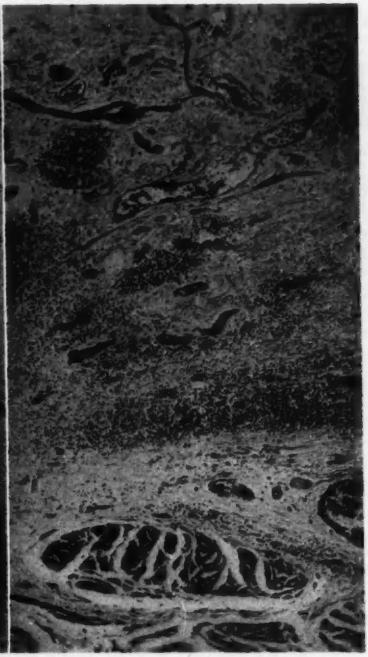


Fig. 6. The area below that shown in Figure 1. The same changes in the submucosa are present and extend down to the muscle.

gross thickening of the bladder wall, although the muscle cells appear hypertrophied. No nerve tissue is recognized. There is a little subperitoneal fat. A moderate number of lymphocytes and neutrophiles are scattered in the edematous connective tissue.

"Summarizing: The outstanding features of the lesion are marked, diffuse, interstitial edema, hemorrhage, and muscular hypertrophy. The epithelium is desquamated completely, and there is a low-grade inflammation. I cannot identify this as a neoplasm, and feel that it is more likely inflammatory.

"Pathologic diagnosis: Edema, chronic inflammation, and hypertrophy of urinary bladder wall with desquamation of epithelium."

Fig. 7. Extension of the process into the bladder wall with the new blood vessel formation between the muscle bundles and fibres. The muscle cells and bundles are healthy and there is no hypertrophy of the muscle cells.

Recovery was more or less uneventful, and since operation the patient's condition has been good except that the bladder has remained infected in spite of rather persistent treatment by Dr. Farber; he has to void every two or three hours during the day. Although the bladder capacity has been only about two hundred cubic centimeters the patient may sometimes not void during the night.

Reëxamination (April, 1941): Urine acid, somewhat cloudy, albumin one plus; cultures showed only Aerobacter aerogenes. Intravenous phthalein test: 40 per cent in thirty minutes.

The urethra and bladder were washed out and the prostatic and seminal vesicular secretions were then shown to contain a good deal of pus.

Cystoscopy showed a moderate bulging of the area of the bladder wall in the region from which the tumor had been removed, that is, between the ureters. There was no ulceration anywhere. The ureteral ridges could not be seen and the ureteral orifices were quite abnormal, the openings were enlarged, round, thin-lipped, and situated on either side of the lower (dorsal) part of the above mentioned protrusion. An elevation of the vesical orifice behind was evident, but perhaps no

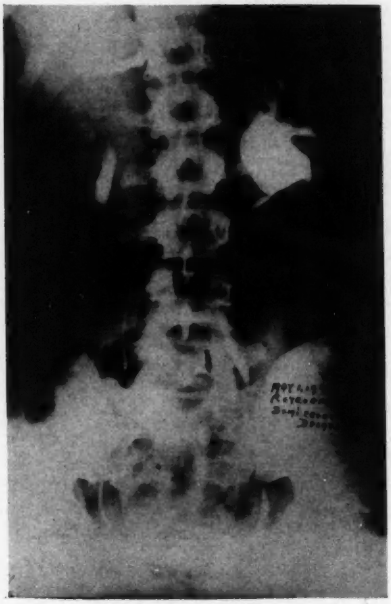


Fig. 8. Retrograde urogram May 1, 1941, a year after operation. Semi-erect position. The roentgenogram was made about thirty seconds after the catheters were withdrawn. The ureters are definitely smaller than before excision of the ulcer.

more marked than it was when seen before operation. The measured bladder capacity was about 200 cubic centimeters.

A 6 F. ureteral catheter passed easily to each kidney. A differential intravenous phthalein test collected for twenty minutes showed right 14 per cent, left 13 per cent, bladder 5 per cent. The urine from the kidneys contained no pus or bacteria.

Twenty cubic centimeters of skiodan were injected slowly into each kidney without producing symptoms. The roentgenograms (Fig. 5) showed the same hydronephrosis of each kidney which was found before but there was very definitely less dilatation of the ureters, and no retention of skiodan in the ureters or in the right kidney at ten minutes after the catheters were withdrawn for the semi-erect roentgenogram. There was a good deal of retention in the left kidney even at twenty minutes, and the stereoscopic urogram showed the left ureteropelvic junction to be above the lowest part of the kidney pelvis.

DISCUSSION

The etiology of this ulcer is to me, at least, obscure. Just when the processes underlying the development of the ulcer appeared it is impossible to say.

There are several things which could be considered as the underlying cause of the ulcer: (1) bladder wall changes of unknown origin which at first caused ureteral obstruction and hydronephrosis and later produced the bladder infection and ulceration; (2) fibrosis about the vesical orifice causing bladder neck obstruction with the development of hydronephrosis and later of a bladder infection and then an ulceration; (3) a hydronephrosis perhaps of congenital origin, and independent of the bladder infection and ulceration, and the ulceration caused by the bladder infection, the lesion being produced, as Schulte suggested, by the special type of organism which happened to infect the bladder.

The hydronephrosis was bilateral at the time of the first pyelogram but at this time, although the urine "contained a little pus," it was uninfected and the bladder and ureteral orifices were reported to be normal. Six months later there was enlargement of the ureters (lantern slides Dr. Young sent me) as well as the hydronephrosis, and the bladder was infected, but the bladder and vesical orifices were pronounced normal. But following the cystoscopy and urogram marked bleeding began and continued for ten days and some bleeding continued intermittently for a month, which suggests that the ulceration, or the processes underlying the ulceration, were already present in spite of the fact that the patient had had no urinary symptoms.

I think that there can be no doubt but that changes in and about the ulcer were causing ureteral obstruction when I saw him and that they were considerably relieved by the removal of the ulcer.

It is interesting that Fenwick in his 1896 article reported that he

had seen the simple ulcer so frequently in young men about twenty, which was the age of this patient, but it does not seem possible for him to have had a simple solitary ulcer which was asymptomatic and which was not seen by Bromberg nor at the cystoscopy done on admission to the Brady Institute. Nor does it seem possible that it was an ulcer of interstitial cystitis, a "large, chronic, elusive ulcer" (as Keyes says about Fenwick's case) because there were no urinary or bladder symptoms present before he went to the Brady Institute.

Perhaps the most acceptable suggestion is that the hydronephrosis was an independent process and that, as Schulte thought happened in his case, the ulceration was produced by either the staphylococcus infection or by both the staphylococcus and the Streptococcus fæcalis bacteria. But in concluding I am compelled to admit that I am not able to explain the cause of the ulcer, the bladder infection, or the bilateral hydronephrosis.

SUMMARY

Bladder ulcers other than those resulting from cancer, syphilis, trauma, and radiotherapy have been reported but not often in the literature. The terms employed to distinguish these ulcers have been varied. We may call them for the time being simple chronic ulcer, perforating ulcer, the ulcer of interstitial cystitis, and incrusted ulcer. To these we should perhaps add an ulcer caused by staphylococcus infection (and perhaps other bacteria) of the bladder.

The etiologic factors mentioned have been trophic changes in the bladder wall, metastatic infection of the mucosa or submucosa, the obliteration of some of the small blood vessels of the mucosa by various processes, and bladder infection with staphylococcus (Schulte) and other organisms. But I am not sure that satisfactory proof has been advanced to establish the exact cause of any of these ulcers.

Schulte reported a bladder ulcer much like the one I found, which seemed to have been caused by a strain of staphylococci which, in experiments with animal inoculation, had a definite tendency to produce urinary tract lesions rather than lesions elsewhere, and in one animal produced an ulcer of the bladder like the one found in his patient.

My case was a young man of twenty who for five years before the ulcer appeared had increased arterial tension, orthostatic al-

buminuria, and general malaise. Eighteen months before I saw him, bilateral hydronephrosis was found but the bladder was normal. Six months later his bladder was infected with staphylococcus and Streptococcus fæcalis but no urinary symptoms were present. He had severe bleeding for ten days after cystoscopy but the ulcer was not seen. About ten months later I found an ulcer on the posterior wall of the bladder, where the wall protruded to overlie the ureteral ridge region. This protrusion was more or less fixed. The ulcer was about five centimeters in diameter, shaggy, with a red base, fairly well defined edges, and elevated a little above the surrounding mucosa. It was excised and a report on the tissue examination is given. I could not decide upon a definite cause for the development of the ulcer.

REFERENCES

1. Buerger, Leo: The pathology and treatment of callous ulcer of the bladder. Med. Record, 83:656-661, (Apr. 12) 1913.
2. Buerger, Leo.: Ulcer of the bladder. Jour. A.M.A., 60:410-421, (Feb. 8) 1913.
3. Cabot, Hugh: Modern Urology, 11:126, 1918.
4. Chamber, G.: Solitary Ulcer of the Bladder. Brit. Med. J., pp. 1019-1020, June 16, 1928.
5. Fenwick, E. Hurry: The clinical significance of the simple solitary ulcer of the urinary bladder. Brit. Med. Jour., pp. 1133-1135, (May 9) 1896.
6. Fenwick, E. Hurry: Handbook of Clinical Cystoscopy. London: J. A. Churchill, 1904.
7. Horine, Cyrus F.: Intraperitoneal perforation of bladder ulcer. Urol. and Cutan. Rev., 36: No. 7, (July) 1932.
8. Keyes: Urology. p. 176. D. Appleton & Co., 1928.
9. Lazarus, J. A.: Simple chronic ulcers of the urinary bladder. Jour. Urol., 34:111, (Aug.) 1935.
10. LeFèvre, H.: Ulcer simple performant de al vessie. Jour. d'urol. méd. et chir. 3:51-54, 1913.
11. LeFur, Renè Frédérick: De l'ulcère simple de la vessie. Thèse. Paris: G. Steinheil, 1901.
12. Ottow, B.: Incrusted vesical ulcers in females. Zentralbl. f. Gynäk, (Oct. 29) 1932. Abstract in Year Book for Urology, p. 242, 1933.
13. Paschkis, Rudolf: Non specific chronic ulcers of the bladder. Urol. and Cutan. Rev., 33: No. 4, (Apr.) 1929.
14. Ruth, A. L.: Bladder ulcer—Unusual type. Penn. Med. Jour., 32:771-772, (Aug.) 1929.
15. Schulte, T. L.: Unusual vesical ulcer. Report of a case. Proc. Staff Meet. Mayo Clin., 16: No. 7, (Feb. 12) 1941.
16. Walker, Geo.: Simple ulcer of the bladder. Jour. A.M.A., 48:1019, (Mar. 23) 1907.

SOLITARY TUMOR-LIKE AMYLOIDOSIS OF THE URINARY BLADDER

CARL F. RUSCHE, M.D. and SAMUEL K. BACON, M.D.
From the Department of Surgery (Urology), University of Southern California School of Medicine, Hollywood, California

A solitary tumor of amyloid in the genito-urinary tract is one of the rarest pathologic lesions in this system of the human anatomy. Localized areas of amyloid are rarely found in any part of the body, except perhaps in the larynx. The literature presents occasional single case reports of local amyloid tumors involving the conjunctiva, cornea, tonsil, tongue, vocal cords, trachea, heart, fallopian tube, skin, and brain.

In general amyloidosis practically every tissue, in some instances, has revealed amyloid. The lesion predominates in the liver, spleen, and kidneys and in these cases it is not unusual to observe amyloid infiltration in several other tissues.

The causative factors of amyloidosis are unknown. Theories predominate and they have been the subject of voluminous debate. It is agreed that amyloid is albuminous degeneration or infiltration and that it usually occurs in patients having chronic wasting diseases or chronic suppurative processes.

In the past year we have had the rare experience of conclusively establishing the diagnosis of amyloidosis of the urinary bladder in two cases. These were solitary tumors. In each case the pre-operative clinical diagnosis was carcinoma; however, after extensive microscopic study of the excised tissue treated with special stains, there was no evidence of malignancy. The tissue revealed amyloid. We present the clinical details of the two personal cases.

Case 1.—A. R., a woman aged fifty-one, was admitted to the Los Angeles County General Hospital on June 11, 1940. She complained of blood in the urine for a duration of three weeks. There was no pain in the bladder or on micturition. Two years previously there was a transient attack of hematuria and the patient's physician "burned a small wart" in the bladder, cystoscopically. There was no history of chronic wasting diseases or chronic suppurative processes. The only recent medical treatment was for "ulcers of the stomach."

On physical examination the patient was a white woman, well developed and well nourished. There were no essential abnormalities other than a soft, systolic murmur at the cardiac apex and a small

urethral caruncle. The systolic blood pressure, expressed in millimeters of mercury, was 130; diastolic, 100. The urine revealed albumin, 2 plus, and erythrocytes, 4 plus; no pus cells or bacteria. One cubic centimeter of phenosulphonephthalein given intravenously appeared in four minutes; 60 per cent and 15 per cent recovered in the first and

Fig. 1. Section of bladder wall through the amyloid tumor which is stained with Congo red. The "island" of amyloid is surrounded and partitioned with lamellæ of fibrous tissue.

second thirty-minute periods, respectively. The value of non-protein nitrogen in the blood was 30 mg. in 100 cubic centimeters of blood. Excretory urograms did not reveal any essential pathologic lesions.

On cystoscopy there was an "infiltrating type of tumor involving the left lateral wall and dome of the bladder." Surgery was advised, ac-

cepted, and carried out on June 18, 1940. The bladder was exposed through a subumbilical incision in the median line and "approximately one-half of the left wall and dome of the bladder were resected, carrying with it all of the pathologic area and an adequate amount of normal tissue."

The surgical specimen measured 6 cm. by 6 cm. by 2 cm., bearing an area of ulceration 3 cm. by 1.5 cm. The cut surfaces did not present the usual characteristics of neoplasm. Microscopically, there was no evidence of malignancy; however, there were extensive inflammatory changes, with cellular exudation, hemorrhage, and mucosal ulceration. The tissue was treated with special stains (van Gieson's, methyl violet, iodine, iodine and sulfuric acid, congo red) and then the pathologist* stated, "a notable feature is extensive areas of amyloid deposit involving smooth muscle, connective tissue, and walls of the blood vessels" (Fig. 1).

The patient recovered; however, the convalescence was complicated by indolent healing of the wound and pulmonary embolism and infarction on the fifth postoperative day. She was discharged from the hospital as well on the fifty-first postoperative day.

Subsequent examinations in the urologic clinic revealed that the patient was enjoying good health. On cystoscopy, the vesical capacity was 250 cubic centimeters; vesical contour somewhat irregular; no evidence of ulceration or neoplasm; urine grossly clear, chemically and microscopically negative. Twenty-nine per cent of an aqueous solution of congo red, given intravenously, disappeared from the blood in one hour. This result was not indicative of general amyloidosis.

A more recent examination (March 27, 1941) revealed that the patient had gained 20 pounds in weight and was in excellent health. There were no urologic symptoms or abnormal findings on examination of the urine. Cystoscopy revealed no residual urine; vesical capacity 600 cubic centimeters; excellent renal function with indigocarmine; ridge of scar tissue on the left antero-lateral wall; few dilated capillaries on the trigone. Two specimens of tissue were removed with the McCarthy visual prostatic electrotome for pathologic study. There was no evidence of amyloid.

Case 2.—N. C., a Caucasian man aged sixty-nine, complained (December 9, 1937) of blood in the urine "occasionally" for the past twenty-five years and almost continuous bleeding for the past three months. There were other complaints of urinary frequency, nocturia, pain on urination, chills and fever.

The patient was admitted to the Los Angeles County General Hospital. Physical examination revealed benign prostatic hypertrophy and tenderness in the left costovertebral angle. The urine was grossly bloody, contained albumin, few pus cells, many erythrocytes, many

*We express our appreciation to Newton Evans, M.D., chief pathologist of the Los Angeles County General Hospital, to V. L. Andrews, M.D., pathologist to the Hollywood Presbyterian Hospital, and to James Ewing, M.D., pathologist to the Memorial Hospital of New York City for their invaluable contributions in the study of the pathologic lesions.

gram negative bacilli and cocci. The residual urine was 15 cubic centimeters. One cubic centimeter of phenolsulphonephthalein, given intravenously, appeared in eight minutes; 30 per cent and 15 per cent were recovered in the first and second thirty-minute periods, respectively.

Cystoscopy revealed a localized, elevated, irregular, ulcerated, hemorrhagic area on the right postero-lateral wall of the bladder. Its diameter was 3 centimeters. The prostate presented early hypertrophy. Indigo-carmine was excreted in five minutes from each kidney in deep concentration. Biopsy specimens were taken of the vesical ulcer. The pathologist reported fibrous tissue—no evidence of malignancy.

On December 23, 1937, biopsy was done and the ulcer was fulgurated transurethrally. These specimens, removed for microscopic study, did not reveal malignancy, The patient improved and was discharged to the clinic.

On February 2, 1938, the cystoscopist reported some evidence of necrotic tissue remaining on the right postero-lateral wall of the bladder. On March 9, May 4, and June 29, 1938, cystoscopic examinations revealed "bladder negative," "no tumor," and "no tumor," respectively; however, on December 15, 1938, another cystoscopist observed a 4 millimeter area of ulceration at the previous site. He concluded that this was "probably recurrent tumor of the bladder." The patient refused admission to the hospital.

After experiencing one month of hematuria, the patient consented to hospitalization on September 21, 1940. Cystoscopy revealed a nodular, localized area of ulceration on the right postero-lateral wall of the bladder. Sections of the excised tissue treated with special stains were reported, after microscopic study, as amyloid. There was no evidence of malignancy. The remaining part of the lesion was fulgurated.

More recently (January 1, 1941) the patient was re-admitted to the hospital. One of us (C.F.R.) removed three deep sections of tissue from the indolent ulcer and resected 8 grams of prostate. The pathologist reported that the vesical sections were "partially covered with transitional epithelium characteristic of mucosa; smooth muscle, much of which is encroached upon by extensive amyloid material; no evidence of malignancy." The prostatic tissue revealed benign hyperplasia; no evidence of amyloid infiltration.

In order to acquaint ourselves with the prevalence of solitary tumors of amyloid in the genito-urinary tract, especially in the bladder, we have conducted an extensive and complete investigation of medical literature (Table I). In 1897, Solomin[17] published the first record "about local amyloid of the bladder." The patient was a woman aged seventy-three years, that presented one solitary plaque of amyloid, 8 cm. in diameter, on the posterior wall of the bladder. Lucksch,[14] in 1904, reported the necropsy finding of amyloid tumors

of the bladder. His patient was a woman, aged forty-two, who had died of chronic pulmonary, intestinal, and laryngeal tuberculosis. The bladder revealed many amyloid tumors of the muscularis, some as much as 2 square centimeters in area and 0.5 centimeters in elevation. In 1932, Chwalla[6] of Vienna published the record of "a case of amyloidosis at the bladder neck resembling a tumor." On cystoscopy the lesion was observed to involve the bladder at

TABLE I. SOLITARY TUMOR-LIKE AMYLOIDOSIS

Bladder	
Solomin	1897
Lucksch	1904
Chwalla	1932
Rusche and Bacon	1941
Rusche and Bacon	1941
Urethra	
von Tilp	1909
Herxheimer and Reinhart	1913
von Albertini	1925
Chwalla	1932
Renal Pelvis	
Akimoto	1927
Seminal Vesicles	
Lubarsch	1929
Ureter	
Lehmann	1937

the internal urinary meatus and in the posterior urethra. Professor Erdheim examined the excised tissue and diagnosed the lesion as local amyloid tumor of the urethra and bladder. The three preceding cases represent the references in medical literature to the subject of amyloid tumors of the bladder.

There are four case reports in the literature of solitary amyloid tumors of the urethra, by the following authors, namely: von Tilp[18] (1909), Herxheimer and Reinhart[9] (1913), von Albertini[19] (Suter's case, 1925), and Chwalla[6] (1932). Further investigation presented the single case reports (three) or local amyloid tumors elsewhere in the genito-urinary tract. Akimoto[1] of Freiberg, in 1927, reported the necropsy finding of amyloid-like deposits in the left renal pelvis; Lubarsch,[13] in 1929, published the record of a patient with localized amyloid deposits in the seminal vesicles; and, Lehmann[11] of Danzig, in 1937, reported in detail the necropsy finding of a "purely localized amyloid" in the wall of the left ureter.

CONCLUSIONS

1. A solitary tumor of amyloid in the urinary bladder is one of the rarest pathologic lesions.

2. Clinically, this lesion is confused with neoplasm; however, readily identified with special stains for amyloid.

3. The literature presents three cases of amyloidosis of the urinary bladder; four cases, of the urethra; and, one case each of the renal pelvis, seminal vesicle, and wall of the ureter.

4. We have presented two cases of solitary tumor-like amyloidosis of the urinary bladder, each substantiated by adequate proof of the pathologic lesion.

REFERENCES

1. Akimoto, K.: Amyloid-like deposits in the renal pelvis. Breitr. z. path. Anat. u. z. allg. Path., 78:239-242, (Aug. 12) 1927.
2. Balyeat, F. S.: Enlarged tongue from amyloidosis. Calif. & West. Med., 43:154, (Aug.) 1935.
3. Budd, J. W.: Primary amyloid disease of the heart and great vessels; Case. Am. Jour. Path., 10:299-308, (March) 1934.
4. Bürgi, U.: Solitary amyloid tumor of parietal bone. Frankfurt. Ztschr. f. Path., 50:410-428, 1937.
5. Chiari, H.: Isolated local amyloid deposit in tonsil. Monatschr. f. Ohrenh., 71:666-670, (June) 1937.
6. Chwalla, R.: A case of amyloidosis at the bladder neck resembling a tumor. Urol. and Cutan. Rev., 36:381-384, (June) 1932.
7. Delarue, J., and Thorel, M.: Amyloid tumor of fallopian tube. Ann. d' anat. path., 15:1050-1054, (Dec.) 1938.
8. Hass, G., and Schulz, R. Z.: Methods of isolating amyloid from other tissue elements. Arch. Path., 30:240-259, (July) 1940.
9. Herxheimer, G., and Reinhart, A.: Ueber lokale Amyloidosis (insbesondere die sogenannten Amyloidtumoren). Berl. klin. Wchnschr., 1:1648-1654, 1913.
10. Jorgensen, A.: Amyloid tumor of larynx; Case. Ztschr. f. Laryng., Rhin., Otol., 25:209-213, 1934.
11. Lehmann, G.: Local amyloidosis in wall of ureter. Zentralbl. f. allg. Path. u. Anat., 68:209-213, (Sept. 15) 1937.
12. Lubarsch, O.: Amyloidosis, unusual sites; three cases. Virchows Arch. f. path. Anat., 271:867-889, 1929.
13. Lubarsch, O.: Localized amyloid deposits in seminal vesicles. Virchows Arch. f. path. Anat., 274:139-145, 1929.
14. Lucksch (Prag): Ueber lokale Amyloidbildung in der Harnblase. Verhandl. d. deutsch, path. Gesellschaft, 7th Session, pp. 34-39, 1904.
15. Musial, A.: Amyloid tumor of the eyelid. Polska gaz. lek., 13:180-181, (March 4) 1934.
16. Paige, B. H.: Myeloma with unusual amyloid deposition; case. Am. Jour. Path., 7:691-700, (Nov.) 1931.
17. Solomin, P.: Ueber locales circumscriptes Amyloid in der Harnblase. Prag. med. Wchnschr. 22:3-5, 1897.
18. von Tilp, A.: Ueber lokales tumorförmiges Amyloid der Harnröhre. Centralbl. f. allg. Path. u. path. Anat., Jena. 20:913-916, 1909.
19. von Albertini, A.: Local amyloid of the urethra. Frankfurt. Ztschr. f. Path., 33:248-257, 1925.

UNUSUAL UROGENITAL CARCINOMATA

LEON HERMAN, M.D.
Philadelphia, Pennsylvania

Pathologic data from the cases to be described were used as the basis of an illustrated talk on the subject of this communication. The case histories and descriptions of specimens will be given in abstract, while only a few of the illustrations originally used will be reproduced. However, complete data are available to those particularly interested.

CASE REPORTS

Adenocarcinoma Involving an Epiplocele, Metastatic from a Primary Rectal Lesion

Case 1.—U. A., Italian, aged 70, was admitted to the surgical service of Dr. John Flick at the Pennsylvania Hospital, March 8, 1941, complaining of diarrhea, oftentimes bloody, of eight weeks' duration. Examination disclosed a large scrotal hernia (R), reducible in so far as its intestinal contents were concerned, but comprising in addition to the latter, two solid masses situated above and in front of the normal testis and without demonstrable attachment to the spermatic cord. The upper mass which was about the size and shape of a Brazil nut, but somewhat irregular in surface contour, was of stone-like consistency and displaceable into the abdominal cavity. The second mass, situated several centimeters below the foregoing with which it had no demonstrable connection, was the size and shape of a plum but otherwise resembled the smaller tumor; it was displaceable to the level of the hernial orifice.

Examination of biopsy specimens confirmed the clinical diagnosis of metastatic carcinoma to an epiplocele, the constituent cells being mucoid in type (Fig. 1). The primary lesion proved to be a dense annular adenocarcinoma which largely occluded the lumen of the rectum.

Comment.—Identification of the nature of the scrotal masses as neoplasms of metastatic origin was not difficult in view of their isolation from the normal scrotal contents, displaceability, and highly suggestive, if not wholly characteristic physical features. However, the masses were thought by a number of examiners to be of primary genital origin. The case is unique in the writer's experience.

Carcinoma of the Scrotal Wall, Metastatic from Gastric Carcinoma

Case 2.—J. M., aged twenty-nine, was admitted to the Urological Department of Pennsylvania Hospital on September 28, 1939, and died in the Jeanes Hospital, December 4, 1939.

Seven weeks prior to admission, the patient discovered a hard, non-tender plaque in the scrotal wall on the right side. When discovered

Fig. 1. Microphotograph (× 110). Surgical specimen No. S. 32127. Biopsy specimen from a nodule in an irreducible scrotal epiplocele showing adenocarcinoma.

the growth was about 1.5 cm. in diameter. It grew rapidly, spreading in all directions to involve the entire scrotum, base of penis and perineum.

Examination disclosed extensive induration of the scrotum and adjacent tissues. The scrotal contents, which could not be identified, formed together with the scrotum a small, stony hard, puckered mass held firmly against the pubic bones. The involved tissues were slightly tender, but otherwise lacking in signs of inflammation. A study of specimens taken from the perineo-scrotal area showed anaplastic carcinoma (Fig. 2).

In searching for a primary lesion, the history of vague digestive disorder of one year duration was elicited and led to the demonstration of advanced gastric carcinoma with an annular neoplasm of the transverse colon. The patient died in the Jeanes Hospital two months later and the autopsy record and tissue sections kindly sent us by Dr. Hastings show that there was primary anaplastic carcinoma of the stomach

Fig. 2. Microphotography. Surgical specimen No. S. 29166. Biopsy specimen showing metastatic carcinoma of the scrotum.

with metastases involving among many other structures, the scrotal wall.

Comment.—With the exception of surprisingly insignificant indigestion, the appearance of a small, indurated plaque in the scrotal wall was the initial symptom of the disease. Demonstration of the neoplastic nature of the scrotal lesion led to discovery of the primary neoplasm.

Carcinoma of Testicle Probably Metastatic from Papillary Carcinoma of the Bladder. Orchiectomy (L) and Total Cystectomy

Case 3.—Dr. W. C., aged sixty-nine, consulted us in 1938 when the following conditions were identified; multiple urethral strictures, severe cystitis, prostatic hyperplasia (commissural), and a cystographic defect suggestive of neoplasm. On re-admission October 10, 1940, the

patient, a Canadian physician, stated that in April, 1940, he was examined by a urologist in Kingston, Ontario, who destroyed by electrocoagulation a small papillary neoplasm of the bladder. This was followed by tender enlargement of the left testicle, in which there is residual swelling and induration. The pre-operative diagnosis was chronic epididymitis and the extirpated organ disclosed what was thought to be suppurative epididymo-orchitis. The pathologic diagnosis

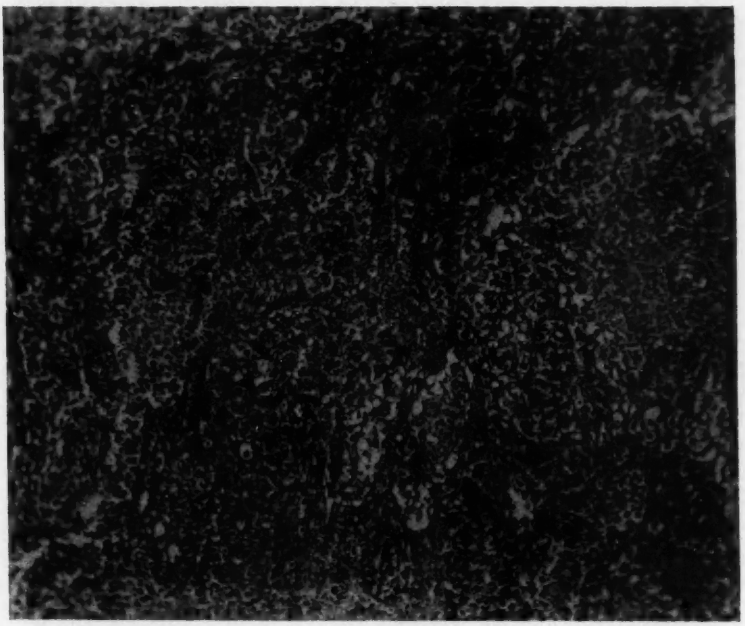


Fig. 3. Microphograph (× 110). Surgical specimen S. 31273. Carcinoma of testicle probably metastatic from vesical neoplasm.

was, "anaplastic carcinoma possibly metastatic from the bladder." This opinion seems to have been based largely on the occurrence in some portions of the tumor of a papillary arrangement of the cells (Fig. 3). The patient at the time was without severe bladder symptoms and the pathologist was entirely unfamiliar with the patient's history. The patient was readmitted January 4, 1941, on account of dysuria and frequency of urination. Cystography revealed a large vesical filling defect caused, as proved by cystoscopic examination, by a large solid neoplasm occupying the left half of the bladder cavity and

extending very near to but not involving the sphincteric area. The left upper urinary tract was moderately dilated.

Operation performed February 14, 1941, consisted of a total cystectomy with cutaneous ureterostomy. The disease was very extensive (Fig. 4) but five months after operation there is no evidence of recurrence or metastases.

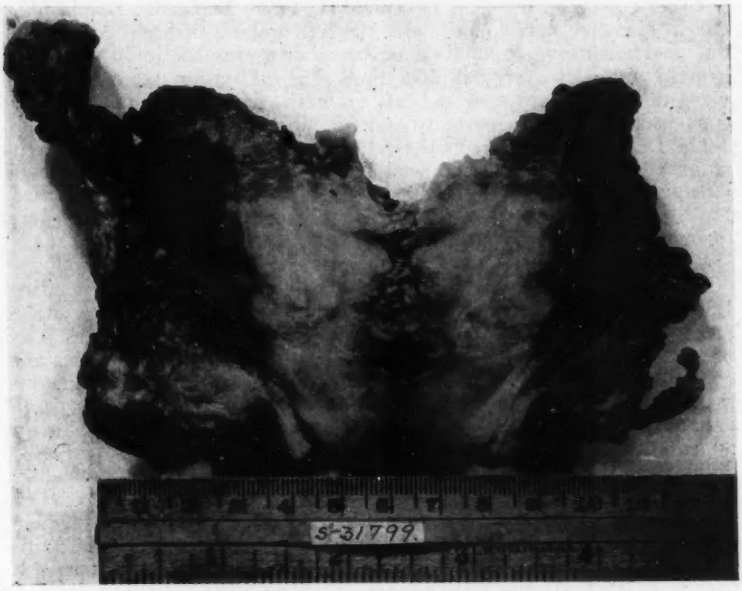


Fig. 4. Extensive carcinoma of the urinary bladder.

Comment.—The testicular neoplasm was in all probability metastatic from the vesical neoplasm. In both instances the cellular arrangement in places was papillary and in the case of the testicle unlike any primary new growth of the organ. The fact that the patient had urethral strictures and advanced cystitis is offered as an excuse for failure to recognize the neoplasm in 1938. There were surprisingly few vesical symptoms in 1940, although the tumor had grown to large size. Six months prior to cystectomy a competent urologist was of the opinion that the neoplasm was small and papillary (benign) in type.

Extensive Infiltrating Carcinoma of the Bladder. Pyonephrosis (L). Marsupialization of Bladder. Suprapubic and Cystoscopic Radon Implantation and Intracavity Irradiation. Nephrectomy (L). Salvaged Twenty-eight Months

Case 4.—J. C., male, aged fifty-five, was admitted to Bryn Mawr Hospital, December 2, 1938. He had painless hematuria for six months, and dysuria. Weight loss was 18 pounds.

Cystoscopy was done on December 5, 1938. Semisolid neoplasm, 2 cm. in diameter, was found above the left ureteral orifice. To right of this and extending to midline of basal area was an infiltrating new growth with deep marginal ulceration. The infiltration extended downward to a point very near the left ureteral orifice. The upper urinary tract was normal to urography and functional tests.

On December 12 marsupialization of the bladder and electrocoagulation of neoplasm was followed by implantation of 15 radon seeds (2 mc. each). In the interval between January 10 and January 23, 1939, six deep x-ray therapy treatments totaling 2520 R. were given through an intracavity cone.

Biopsy specimen removed at operation was described as follows: "Specimen—grayish tumor, probably a papilloma with base measuring 1.5 x 1 x 1 cm. Tumor is rather friable and section surface shows striæ radiating from the base. The section is composed almost entirely of highly atypical epithelial elements occurring in irregular masses and columns. The presence of a regular fibrous and vascular stem suggests that this was originally a papilloma; indeed, in certain ones the papillomatous arrangement is fairly well preserved. The base of the tumor appears infiltrated at the periphery. The cellular elements are highly atypical and mitotic figures very numerous."

Diagnosis: Carcinoma of the bladder.

On February 13, 1934, the bladder wound was closed. A segment of bladder wall at the previous site of neoplasm was removed; this showed no evidence of active carcinoma. The patient was discharged March 2, 1939.

The patient was readmitted on account of headaches on February 23, 1940. Examination showed an elevated neoplasm (1 x 2.5 cm.) obscuring the left ureteral orifice, and another (0.5 cm.) lateral to and slightly above the former.

Two biopsy specimens were removed. One of these was covered with modified squamous epithelium. The bulk of the tissue was formed of nests of very highly atypical squamous epithelium showing marked distortion and degeneration with extensive vacuolization. Numerous nests of cells appeared vital and actively growing. The second specimen was alveolar in architecture, showing occasionally a tendency to palisade formation with cylindrical cells.

On March 1, 1940, neoplasms were destroyed by electrocoagulation. Five days later the left kidney, which was functionless, was removed. The patient was discharged March 22, 1940, and was admitted again

May 19, 1940. Implantation of 5 radon seeds (1.5 mc. each) was made into the stellate scar at the previous site of recurrent tumor. Reports made December 13, 1940, and May 15, 1940, show the patient to be in good health, with no evidence of recurrence.

Comment.—It would seem that irradiation as originally applied served to destroy the major portion of the extensive infiltrating growth in this case. The relative parts played in the process by radium and roentgen therapy cannot be estimated, but it is reasonable to hold that these rather than electrocoagulation were effective. Reaction from irradiation rather than neoplastic extension probably accounted for ureteral occlusion leading to death of the left kidney. It is my belief that intracavity irradiation accurately applied to certain basal tumors is a useful measure, but one probably best applied to supplement radium therapy. It may, however, if applied directly to the region of an ureteral orifice lead to its occlusion. The tissue sections show marked variability in cellular structure and arrangement due in part to the effects of irradiation.

Squamous Cell Carcinoma of the Renal Pelvis with B. Proteus Pyelonephritis. Postoperative Empyema (B. Proteus). Salvaged Thirteen Months

Case 5.—C. C., male, Italian, aged forty-seven, was admitted to the urologic service of the Pennsylvania Hospital on April 13, 1940, on account of "chills and fever" of two weeks' duration, and a sudden attack of severe pain which began twenty-four hours before admission. The pain, which he localized to the lower lateral portion of the chest on the right side, was associated with nausea and vomiting. Briefly, the examination disclosed bilateral renal infection (Friedländer's bacillus), moderate decrease in function of the left kidney (10 per cent of phenolsulphonephthalein from the left kidney—15 per cent of the dye from the right kidney in fifteen minutes), and rather poor urographic outlines of the minor calices on the right side. Various members of the sulfanilamide group of drugs were used without apparent effect, but the symptoms subsided promptly after pelvic lavage and daily intravenous injections of 2,000 c.c. of glucose solution (10 per cent). The patient was discharged symptom-free (except for pyuria) to the outpatient clinic on May 28, 1940. Here he was followed for four months during which time he developed a boring type of pain in the right loin, occasional attacks of hematuria and fever, and frequency of urination. The appetite was poor and there was progressive loss of weight. A secretory urogram made September 13, 1940, failed to visualize the right kidney, and the patient was returned to the wards. Examination now disclosed bilateral upper urinary tract infection (B. proteus), functionally sufficient left kidney—functionless right kidney

Fig. 5. Surgical specimen S. 31175. Section surface of kidney showing extensive squamous cell carcinoma.

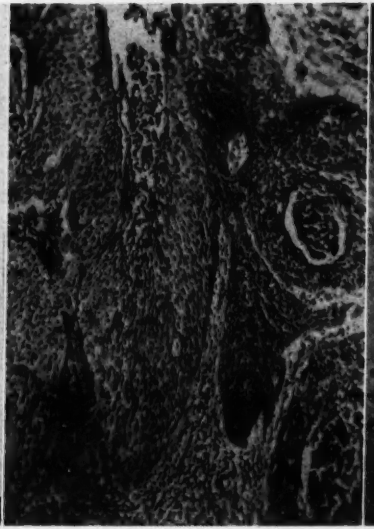


Fig. 6. Microphotograph (× 135). Squamous cell carcinoma of the renal pelvis. (See Figs. 5 and 7.)

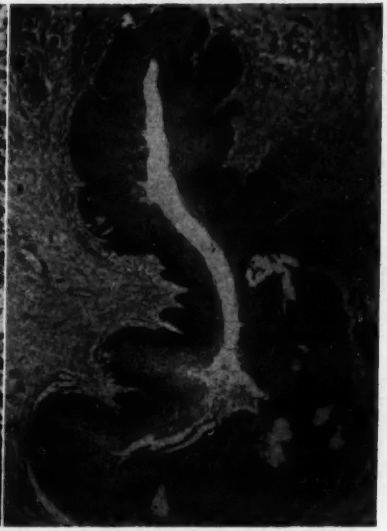


Fig. 7. Microphotograph (× 55). Advanced metaplastic changes in the ureteral mucosa in case of squamous cell carcinoma of the renal pelvis. (See Figs. 5 and 6.)

with impassable ureteral obstruction 26 cm. from the bladder and ureteral filling defects. Right nephrectomy was done September 26, 1940. Difficult removal of a densely adherent, stony hard renal mass weighing 420 gms. (Fig. 5).

Pathologic Diagnosis: Squamous cell carcinoma of the renal pelvis. Figure 6 illustrates the architecture of the pelvic neoplasm, the constituent cells of which are epidermoid in type and classified by Dr. Norris as squamous cell. The mucosa of that portion of the ureter adjacent to the pelvis presents characteristic stratified squamous epithelium. Figure 7, which is assumed to be of metaplastic origin and probably the counterpart of the pelvic epithelium whence the tumor originated.

The patient was discharged in rather poor general condition but with wound firmly healed on October 21, 1940. He was readmitted November 20, 1940, and operated upon for empyemia (R) of Bacillus proteus origin. Recovery was uncomplicated. The patient is now in good sealth and has gained 40 pounds in weight.

Comment.—This case conforms in most respects with the eighty-two reported cases of squamous cell carcinoma of the renal pelvis. Infection or calculi are found in association in the proportion of 40 and 50 per cent, respectively. These lesions may occur together while leukoplakia is a not infrequent finding. This case, like the majority, occurred in the fifth decade. In keeping with general experience, the lesion went unrecognized; in fact, no clinician has succeeded in making the correct diagnosis pre-operatively. Rapid development of ureteral occlusion is not unique, and while the same is probably not true of associated B. proteus infection, this is rare. It remains to be seen if this patient succumbs to neoplasm. In no reported instance has the patient survived the five-year period without recurrence; the majority die within a year or two. It remains to explain the ureteral filling defect; squamous cell tumors, unlike the papillary type, are supposed not to implant themselves at lower levels.

Anaplastic, Rapidly Growing, Prostatic Carcinoma Confined (Grossly) to the Left Lobe

Case 6.—J. C., aged sixty-five, presented himself March 26, 1941, complaining of severe dysuria, great urinary difficulty, severe pains in the groin when straining to void, and frequency of urination. The patient stated that his troubles were of three months' duration, prior to which he considered himself perfectly well.

Rectal examination revealed a large tumor mass confined apparently to the left side of the prostate gland. The mass was oval, smooth, uniformly firm in consistency and not tender. It bulged the rectum mark-

edly, and extended upward beyond the reach of the finger. On cystoscopic examination, it was determined that distortion of the vesical outlet was confined to its left half, the mass having invaded the vesical cavity for a distance of approximately an inch and a half. There was no evidence of inflammation, ulceration or edema.

The tumor was incompletely enucleated with considerable difficulty by the suprapubic route. Hemostasis was accomplished by suture and

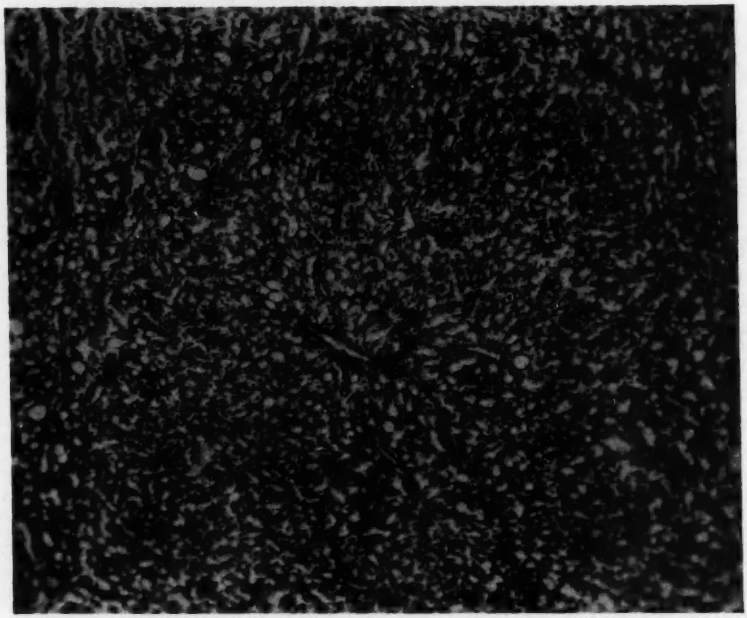


Fig. 8. Microphotograph (× 110). Surgical specimen S. 32242. Anaplastic carcinoma of the prostate gland.

bag. Six days after operation, 2 radium capsules were placed in a hemostatic bag, and this was applied for a period of twenty-four hours to the tumor bed. A course of deep x-ray therapy is now in progress. Figure 8 illustrates the architecture of the neoplasm, description of which follows:

"The tissue is composed of large sheets of an anaplastic malignant epithelial tumor and strands of fibrous trabeculæ and scar. There are no structures which alone would identify the organ as prostate. The tumor is composed of sheets and irregular small pseudo-acini of epi-

thelial cells which are variable in size and shape. Many of the nuclei are hyperchromatic and mitoses are numerous. There is, however, little accompanying reticulum. Fresh areas of necrosis and small abscesses are also present. The irregular scars are associated with deposits of yellow brown pigment, cholesterin crystals, and chronic inflammatory exudate. The absence of visible tumor in the perivascular and perineural lymphatics about the periphery of the tissue does not

Fig. 9. Pyelogram showing defect (indicated by arrow) caused by papilloma originating in a minor calix. (See Fig. 10.)

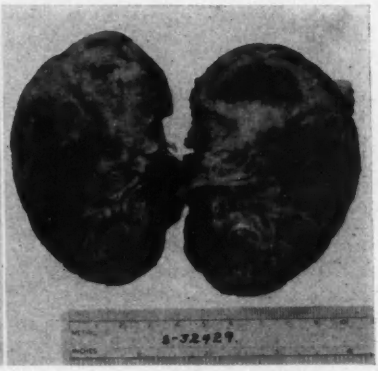


Fig. 10. Section surface of kidney showing papilloma which originated in a minor calix. (See Fig. 9.)

necessarily signify the absence of such permeation in a tumor so anaplastic."

Comment.—In so far as the gross characteristics of the neoplasm are concerned, this case is unique in our experience. It was thought to be an unusual type of benign prostatic hyperplasia, although the possibility of sarcoma or abscess was considered. There was no evidence of metastasis to the lungs or elsewhere. The probabilities are that the perineal approach—whatever the adopted operative procedure—would have had certain advantages, although a mechanically successful radical prostatectomy could not have been accomplished on account of the high extension of the tumor mass. The neoplasm is of epithelial origin and highly anaplastic. There was invasion of the right lobe of the prostate, although this could not be demonstrated by rectal or instrumental examination.

Papillary Carcinoma Originating in a Minor Calix

Case 6.—M. R., aged sixty-six, a white woman, was admitted April 20, 1941, with the history of an initial attack of gross hematuria with dysuria and frequency of urination on the day before admission. This was followed after six hours by intermittent pain in the right flank. Physical examination disclosed slight tenderness in the right flank, moderate cardiac enlargement and a loud systolic murmur at the base. The blood pressure was 180/110. The urine contained a large amount of blood and was sterile. Blood studies disclosed the following: Hemoglobin 57 per cent, red blood cells 4,000,000, white blood cells, 15,000, blood urea nitrogen, 23 mgs., sugar 17.6 mgs. per cent. Total—phenolsulphonephthalein 45 per cent.

Cystoscopic examination localized the bleeding to the right kidney which showed slight dysfunction. The pyelogram (Fig. 9) disclosed a deformity interpreted as neoplastic involvement of a minor calix. A blood transfusion was given on April 30, 1941, and on May 1 the right kidney was removed. The organ was grossly normal with the exception of a small area of softening at the upper pole. A second blood transfusion was given immediately the operation was concluded. Convalescence was uneventful. Section of the kidney disclosed a papillary neoplasm (Fig. 10) filling a minor calix and extending to the isthmus of the associated major calix.

DISCUSSION

DR. BENJAMIN S. BARRINGER (New York, N. Y.): Speaking of marsupialization of the bladder, I have tried in one case the Chaour treatment with the Phillips machine, which is the same thing, a case of hopeless, infiltrating carcinoma of the bladder, and I gave about three times the dose that was supposed to be necessary to control a tumor of the bladder.

He died within a month or so of kidney infection, and we performed an autopsy. It is extraordinary how little work we did on that tumor. Its effect had gone about 1/50 of a centimeter deep and from thenceforth on, I gave up the Chaour treatment of bladder tumors. I think if you could use deep x-ray therapy instead you might get somewhere.

THIRD DAY, MAY 31, 1941

INTRAVESICAL RESECTION OF THE BLADDER WALL AND PERITONEAL COAT FOR CERTAIN BLADDER TUMORS

HUGH H. YOUNG, M.D.

From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital, Baltimore, Maryland

In a recent case I found it possible to do a still more radical operation for tumor of the bladder by extending my technique for suprapubic transvesical removal of the bladder wall surrounding a vesical tumor with the peritoneal coat.

A man, aged sixty-eight, entered the Brady Urological Institute three years after he had undergone left nephro-ureterectomy elsewhere. A papillary tumor of the pelvis of the kidney and ureter had been recognized and through two incisions the kidney and ureter had been removed down to the posterior wall of the bladder. The operative note stated that the ureter had been isolated to the point where it entered the bladder wall, was then clamped, cut off and ligated. The convalescence was satisfactory, but in a short time the patient began to have hematuria.

On cystoscopic examination the instrument entered easily and found about 50 c.c. residual urine. The bladder capacity on forced distention was 250 c.c. The tonicity was good. Study of the vesical orifice showed a rounded lobe in front which was continuous with an enlargement of the right lateral lobe. The posterior margin of the prostate was elevated in the form of a slight bar. The left margin showed very little enlargement, but when the instrument was drawn into the urethra a small rounded left lateral lobe was visible, although not so large as the hypertrophied right lateral lobe which extended well down into the prostatic urethra. At the left corner of the trigone a globular tumor about 2 cm. in diameter was seen. It had a short thick pedicle which sprang from the region of the left ureteral orifice. The surface of the tumor was irregular, somewhat strawberry-like in appearance. There was one small area of hemorrhage and a few bits of adherent mucus but no ulceration or necrosis. The adjacent bladder wall was hyperemic and elevated for a short distance. The right ureteral orifice was normal, but external and posterior to it was the orifice of a small diverticulum.

On rectal examination the prostate was slightly enlarged on both sides and slightly indurated. Both seminal vesicles were apparently normal.

Study of the case showed that whereas nephrectomy and ureterectomy had been complete to the posterior surface of the bladder, it had

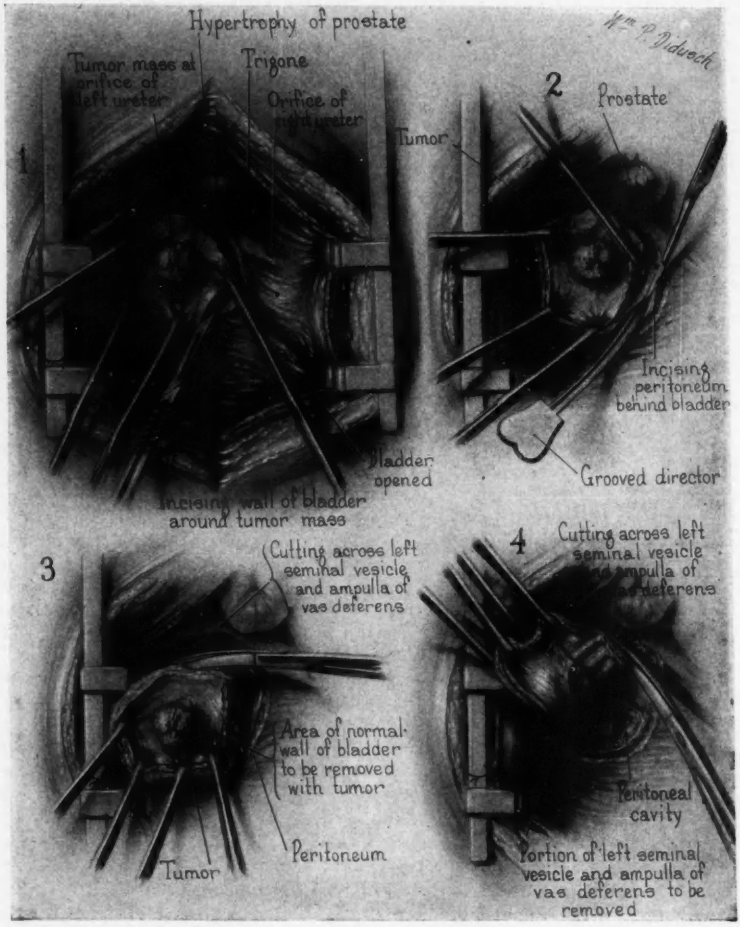


Fig. 1. Details of operation to remove carcinoma of intravesical portion of ureter, adjacent bladder wall and seminal vesicle beneath it. *(1)* Incision around four clamps placed to elevate bladder wall. *(2)* Incision carried through peritoneum. *(3)* Incision carried downward and outward across middle of left seminal vesicle, upper portion of which was left attached to region of ureter. *(4)* Completion of excision of tumor mass with peritoneum and half of seminal vesicle. BUI 29169.

not been sufficient to cure the papilloma which continued to grow within the small terminal part of the intravesical ureter and presented a papillomatous mass in the bladder. In considering the technique to be employed for the operative removal of the tumor, it seemed to me that the intravesical approach would give a better chance for radical removal than a retrovesical or intraperitoneal approach.

On March 25, 1940, under spinal anesthesia, the operation was done. Through a long suprapubic incision, my four-bladed self-retaining retractor was introduced and opened. It afforded a splendid view of the interior of the bladder (Fig. 1). The cystoscopic diagnosis was confirmed. The right ureteral orifice appeared normal. Exactly opposite it a papillomatous tumor about 1.2 cm. in diameter sprang from the bladder wall, having come through the left ureteral orifice into the bladder. The pedicle of the tumor was about 1 cm. in diameter. The adjacent bladder wall appeared not to be infiltrated but it was evident that for radical cure a wide resection should be carried out. The mucous membrane was grasped in four places by Allis clamps (Fig. 1) and an incision made external to them so as to excise a circular area of bladder wall 5 cm. in diameter and about 2 cm. distant from the tumor everywhere. The incision was carried through the mucosa, submucosa and muscle until the peritoneum was opened at a point above and internal to the tumor. Here the seminal vesicle came into view; it lay between the peritoneum and the posterior wall of the bladder. It seemed to be in close proximity and probably adherent to the bladder in the region of the tumor. I decided to carry the resection through the seminal vesicle and vas deferens and to remove these structures above the point of division in one piece with the bladder tumor, surrounding bladder wall and peritoneum (Fig. 1). Bleeding points were seen, clamped and ligated. No difficulty was experienced in continuing the incision around to the outer side of the tumor, going through the structures deeply and dividing the vas deferens above and external to the tumor where it coursed along the posterior wall of the bladder on its way to the epididymis (Fig. 1). The specimen, which included the tumor and an area of entire bladder wall about 5 cm. in diameter, was removed in one piece. The peritoneal coat was present along the inner half of the specimen which included a large portion of the left seminal vesicle and vas deferens along the outer half of the specimen and tissues surrounding the point of division of the ureter at the previous operation. After all bleeding points had been clamped and ligated, the edges of the peritoneum were caught up with clamps and closure effected with a continuous plain catgut suture (Fig. 2). The bladder wound was then closed with a continuous plain catgut suture which embraced the musculosa, submucosa and mucosa. As all retrovesical hemorrhage had been stopped, the posterior bladder wound was closed without drainage.

Examination of the prostatic orifice showed rounded lobes in front and on each side. These were easily enucleated. The larger measured

about 2.5 cm. in diameter. Hemorrhage was controlled by inserting a Foley bag catheter, blowing it up and making traction from without. The anterior wound into the bladder was closed with a continuous chromic catgut suture with a catheter drain emerging from the upper

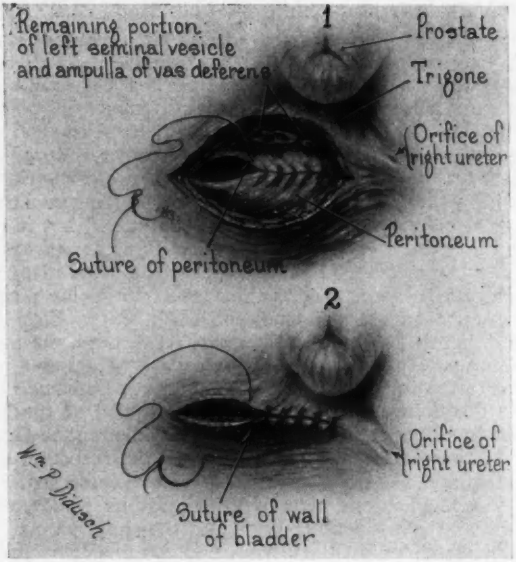


Fig. 2. Closure of defect caused by resection of bladder wall along with terminal portion of ureter, seminal vesicles and overlying peritoneum. *(1)* Approximation of peritoneal edges. (Hypertrophied prostatic lobes, subsequently enucleated, are shown.) (2) Approximation of cut edges of bladder. BUI 29169.

angle. Two Penrose drains were placed in the suprapubic space, and the external wound closed with interrupted sutures of silver wire which included skin, fascia and muscle. The patient stood the operation well.

The specimen consisted of an area of bladder well surrounding a papillary tumor 1.5 cm. in diameter and projecting about 8 mm. above the level of the bladder wall (Fig. 3). In the center of the cauliflower-like mass, there was a small opening which admitted a probe for 2 cm. This was evidently the ureter. On the posterior surface of the bladder wall the upper portion of the seminal vesicle about 1 by 4 by 5 cm. in size, was present; along the inner edge, the vesical portion of the vas deferens, 2 cm. long, was seen. Adjacent to these structures was tissue composed of fat and fibrous tissue. Section through the tumor along the short course of the terminal portion of the ureter showed pale gray

columns which appeared to invade the adacent bladder wall for a short distance, but this did not extend along the outer coat of the bladder, and the structures behind the bladder, seminal vesicle and peritoneum showed no evidence of invasion. The terminal portion of the

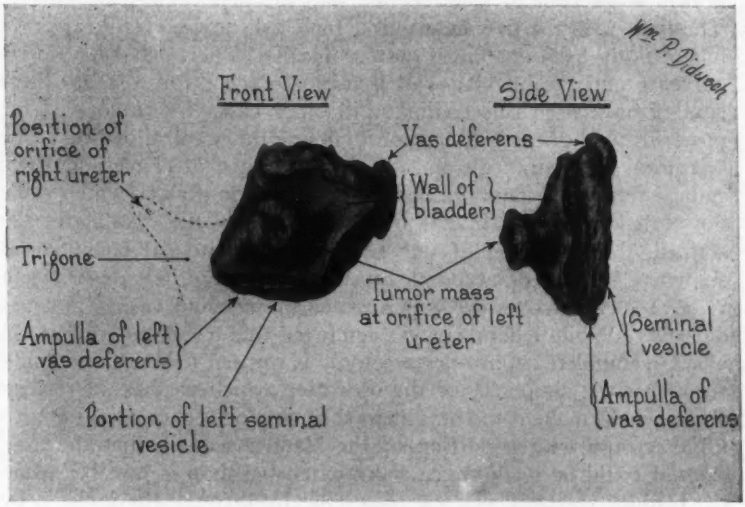


Fig. 3. Drawing of specimen removed at operation. BUI 29169.

ureter had been completely removed. Three lobes of adenomatous prostatic hypertrophy had been removed and on microscopic examination showed benign adenoma. Stained sections of the tumor showed papillary carcinoma which had been completely removed. The deeper tissues, bladder wall, seminal vesicle and peritoneum were apparently not invaded. Impression: The prognosis for a radical cure appeared good.

Discharge note (May 7, 1940): "It is now six weeks since operation in which a portion of the bladder and the terminal portion of the left ureter and left seminal vesicle were removed in one piece, and three prostatic lobes were enucleated. After a short period of bleeding the convalescence was satisfactory. There has been no suprapubic leakage for six days. The patient voids freely at intervals of two to three hours. On rectal examination the prostate is not enlarged; there is slight induration in the remaining portion of the left seminal vesicle; the right seminal vesicle feels normal; the base of the bladder and pelvis are negative. The general condition of the patient is excellent. The urine is clear."

Letter (fourteen months after operation): "I feel as well and as fine as I ever have in my life."

DISCUSSION

The operation we have described above is simply an extension of the technique for transvesical radical removal of bladder tumors with a large area of bladder wall and the peritoneum covering it. The patient in the first case that I reported, now eleven years ago, has recently been examined cystoscopically. There has been no recurrence and the bladder wall is normal except for a small linear scar. I have used this technique in other cases for tumors of the posterior wall of the bladder not involving the ureteral orifices. The operation is not difficult and appears to be the ideal method for a radical removal of tumors in that region. For tumors which come down the ureter and invade the bladder, as in the case above described, the extension of our transvesical peritoneal technique is shown to be easy of accomplishment, even where it is desirable to remove such retrovesical structures as the seminal vesicle and vas deferens. While I have not yet employed this technique in cases in which a complete nephro-ureterectomy is rquired for tumor, it would seem that the simplicity of the operation which we have described above would make it the best method to employ for complete nephro-ureterectomy with a portion of the bladder wall in that the area excised could be made much more extensive than is possible when the bladder resection is done retrovesically through the incision by which the ureter has been exposed. It also has the advantage that it is possible to remove the seminal vesicle and the adjacent vas deferens, which may easily be invaded by the tumor. By this technique it is possible to do a much more radical procedure than by methods heretofore employed.

CONCLUSIONS

The importance of removing the peritoneum covering the wall of the bladder in resections for tumor of the posterior wall of the bladder has been stressed. Without first going into the peritoneal cavity, it has been shown possible to operate entirely intravesically after a wide median line suprapubic incision and the insertion of my four-bladed self-retaining retractor. This gives such a wide exposure of the bladder that it is easy to pick up the mucosa at points quite distant from the tumor and to excise the entire bladder wall with its peritoneal coat and close the defect extraperitoneally through the bladder. It has also been shown in the case reported in

detail that this same technique may be effectively employed to remove a ureteral tumor which has grown into the bladder. In this case not only was the peritoneal covering of the bladder wall removed, but also the terminal portion of the vas deferens and the upper two-thirds of the seminal vesicle which was adherent to the bladder in the region of the tumor. By this extension of the technique a much more radical excision has been accomplished without in any way making the operation more difficult. The procedure is offered as a much more radical technique for the treatment of certain tumors of the posterior wall of the bladder and also of the intravesical portion of the ureter.

REFERENCE

YOUNG, HUGH H.: Treatment of certain vesical neoplasms by intravesical resection of entire bladder wall with peritoneal coat. Jour. Urol., 23:269, 1930.

CANCER OF THE PROSTATE

DIFFICULTIES IN THE EVALUATION OF TREATMENT

H. C. BUMPUS, JR., M.D.
Pasadena, California

Four years ago a physician, sixty-seven years of age, came into my office complaining of the classical, but mild, symptoms of prostatitis. His prostate was moderately enlarged and felt benign upon rectal palpation. The bladder contained 90 c.c. residual urine. Operative interference did not seem imperative, and I told him its indications seemed to me to be based entirely on the severity of his symptoms. He replied that since retiring, it was his custom to spend his summers in a cabin in the northern Vermont woods—and that its inaccessability made him fear an attack of acute retention. Although his present symptoms were not too annoying, he asked that I perform a transurethral resection in order that he might more completely enjoy his vacations. I complied, removing 15 grams.

Nothing in the gross appearance of this tissue suggested any diagnosis other than fibro-adenomatous hypertrophy. You may well imagine my distress, upon receiving the pathologist's report, to learn that the tissue removed was malignant. As this evidently was a very early case, I felt compelled to inform the doctor of the findings. I have seldom had a more distressing task to perform. He had recently given up an active and successful practice in a large eastern city and was looking forward to a well deserved and happy retirement. Now he was to realize that the joys of anticipation too frequently surpass those of realization.

I told him there were certain surgeons whom I greatly esteemed who believed that these early cases could be cured by radical perineal surgery; that at our local California Institute of Technology, Dr. Seely Mudd felt certain that if they did not cure patients by deep x-ray therapy, they certainly arrested its growth in many cases; that in New York at the Memorial Hospital it was believed that in possibly 10 per cent of the vast number of cases treated there with radium, cures had resulted.

He asked me what I thought, and I was forced to reply that in my experience, once a diagnosis was made of cancer of the prostate the possibility of cure was most remote, and that the more rad-

ical methods of surgical treatment seem to involve risks that were greater than hope of cure; that untoward reactions from x-ray and radium were known to have produced great suffering, and that the disease was of slow growth and frequently free of much discomfort if urinary obstruction was relieved.

I explained that occasionally small areas of malignancy were discovered in excised glands and that even then cures did not invariably follow, but only occasionally, due to the fact that the perineural lymphatics from the prostate had been shown to drain not alone along the usual lymphatic routes to regional nodes but directly into the sacrum and pelvis. This finding explained why Kahler found that 51 per cent of all cases of cancer of the prostate diagnosed clinically or on gross examination at postmortem have metastasized, and that in a study of 195 cases he could find no relationship between the size of the carcinoma and the incidence of metastasis.

I told him that I felt I did the greatest good to the largest number in relieving them of their urinary obstruction by transurethral resection without subjecting them to grave surgical risks; that in many cases I had seen attempts at cure of the malignancy result in greater suffering than the disease usually produced and that I doubted any surgical procedure was justified when the operative mortality was greater than the possibility of cure. He said he felt the same way, and then I regretted more than I like to admit that I had informed him of his true condition.

Several years passed, and he again developed symptoms of obstruction, and a subsequent resection was done. The tissue removed was reported benign at this time. The original tissue was reexamined by other pathologists and was also reported to be benign. Naturally, I deeply regretted having caused a fellow physician the mental anguish of believing for three years that he was doomed to die of cancer. At the same time, I was keenly disappointed that I had been deprived of reporting a case of cancer of the prostate cured by transurethral resection, for my friend gave every indication of long life expectancy.

You may well ask, "Why does he burden us with this recitation? We all know that even pathologists can make mistakes, and surely a single case, regrettable as it is occurring to one of our group, proves little." This is a just criticism, were it not for the fact of its greater application and, I now believe, its more general occurrence.

In 1932 and 1933, while a member of the Mayo Clinic Staff, I resected thirty-six patients with cancer of the prostate. The tissue removed was sectioned, routinely examined microscopically, and reported to be malignant. Three years later my former associate, Dr. Gershom Thompson, discovered that eleven of these patients were still living.

Before reporting the fact that nearly a third of these unselected cases of cancer of the prostate survived over a three-year period following resection, he had the tissue removed reëxamined. In two of the eleven cases the first pathologic report had been in error—the tissue removed was, in fact, benign and not malignant. Now, after a lapse of eight years he received, on January 31, 1941, a letter from a member of the original group of thirty-six stating that at eighty-three years of age he weighed 170 pounds and had just finished digging and cutting up a very large apple tree which he had planted fifty years previously. The tissue removed by transurethral resection in this case was also reëxamined and found to be malignant.

Could the other two cases, presumably alive, since they were benign, be added to the case of this hardy individual, the final results for routine transurethral resection in unselected cases of cancer of the prostate would indeed be remarkable.

That such errors may happen to other surgeons and occur in other clinics was forcibly brought to my mind several years ago, when a fellow urologist confided to me that his pathologist was finding that 33⅓ per cent of all his resection cases were malignant. I feel confident that if he has not changed pathologists, some very favorable reports of the cure of cancer of the prostate by transurethral resection will come from his clinic.

In 1939, Kahler made a pathologic study of cancer of the prostate, and his findings, I think, will go far toward reducing what is apparently a frequent error in the microscopic diagnosis of this disease. He writes as follows:

"The microscopic diagnosis of prostatic carcinoma, as for other tissues of the body, depends (among other things) on such criteria as undifferentiation of cells, loss of polarity, and invasiveness and avidity for basic dyes. There is, however, one criterion, which may be peculiar to the prostate gland, that supersedes all others: perineural lymphatic involvement. While extension of a carcinoma to a perineural lymphatic lying in its path is not by any means restricted to prostatic carcinoma,

the abundance of sympathetic fibers within and particularly around the prostate gland and the apparently ideal conditions for growth of prostatic carcinoma in the lymphatics surrounding these fibers forms a definite basis for its malignancy. The absence of these lymphatic vessels in some areas of carcinoma is outweighed by the fact of the uniformity of their involvement in the case of tumors of questionable or of a low grade of malignancy. . . . Extension to the perineural lymphatics was found in the same low-power microscopic field as the tumor in 100 per cent of the cases of grades III and IV tumors, in 85 per cent of those of grade II tumors, and in 87 per cent of those of grade I tumors, of a total involvement of 91 per cent. . . . The localized tumors, many of which were small enough to occupy only one or two low-power microscopic fields, showed as high an incidence of perineural lymphatic involvement as large tumors involving the entire prostate gland. It is evident, therefore, that local removal of the tumor itself, either by transurethral resection or suprapubic prostatectomy, does not eradicate all of the tumor tissue even in the case of neoplasm of a low grade of malignancy."

It would seem advisable, therefore, from the experience here cited, not only to reëxamine the tissue first removed from cases of cancer of the prostate, but to make sure that perineural lymphatic involvement has not occurred before reporting an apparent cure in this disease.

THE EFFECTS OF ESTRADIOL DIPROPIONATE AND DIETHYL STILBESTROL ON MALIGNANT PROSTATIC TISSUE

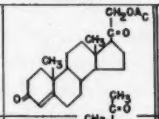
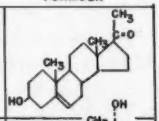
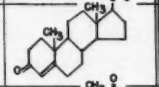
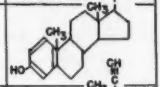
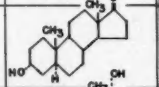
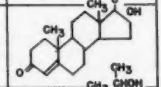
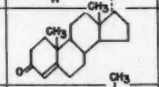
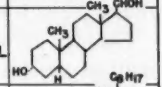
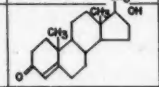
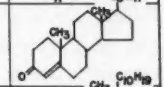
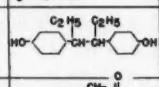
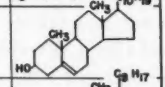
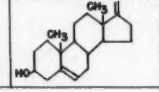
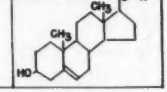
WILLIAM P. HERBST, M.D.
Washington, D. C.

This problem is fundamentally one of biologic chemistry and therefore quite complicated and not remotely near the realm of satisfactory comprehension. The most promising aspect is the observation of varying degrees of selectivity and specificity in action of certain biochemical substances on certain tissues. It seems as if it might be possible to assume that substances which influence vital physiologic function of specific tissues have some chance of modifying processes in malignant tissues which develop in these specific tissues.

Observations in the field of biochemistry in animal research and clinical therapeusis are very numerous and appear to furnish a foundation for countless intelligent and objective projects.

Scapier states that cholesterin is a primary substance of the human organism which is present in all tissues, fluid and cells of the latter, contrary to the so-called secondary substances like glycogen pigment, et cetera, which are not found in all living cells. He emphasizes the fact that any treatment of malignancy should have as one objective the maintenance of a low cholesterin content soil. Mattick demonstrated immediate drop in blood cholesterol content in 95 per cent of thirty-six cancer patients subjected to irradiation. He believes that cancer is characterized by defective lipolysis and cholesteremia. Diener states that the cell membrane is composed of a lipoid mixture and phosphatides, in which cholesterin and lecithin predominate. Between these two there exist certain antagonisms; for example, lecithin causes a decrease of resistance of red corpuscles, while cholesterin counteracts hemolysis. Colloidal cholesterin exerts a lethal effect upon injected animals, while in combination with lecithin it is not injurious. The cholesterin-lecithin ratio should therefore be of vital importance for permeability of cell membrane. He believed that the reason for the radiosensitivity of cells must be labilization of lipoids by roentgen rays (Roffo and Correa, quoted by Diener, assert that roentgen rays appear to exert

their maximum effect upon lipoids, and among the latter upon cholesterin in particular). Charpy declares that the original cause of cancer resides in the disturbance of metabolism of lipoids, particularly cholesterol, resulting in the induction of heterodox mitoses. He used saponin in mice to control malignancy through saponifying cholesterol. Georgine Luden, in 1922, advocated dietary choles-

COMPOUND	FORMULA	COMPOUND	FORMULA
DESOXYCORTICOSTERONE ACETATE		Δ^5 PREGNENE-3(β)-OL-20-ONE	
PROGESTERONE		α-ESTRADIOL	
ANDROSTERONE		ETHINYLTESTOSTERONE	
TESTOSTERONE		PREGNANE-3(α),20(α)-DIOL	
METHYLTESTOSTERONE		Δ^4-CHOLESTENONE	
DIETHYLSTILBESTROL		STIGMASTEROL	
Δ^5-DEHYDRO-ISO-ANDROSTERONE		CHOLESTEROL	

terol control measures as one means to retard cancer. These references are but a few now current in this field.

The striking similarity in the chemical base of steroid hormones is demonstrated by the accompanying table in an article on the "Anesthetic Effect of Steroid Hormones," by Hans Selye.[14]

Note that with the exception of diethyl stilbestrol they are basically similar to cholesterol. Testosterone propionate and estradiol dipropionate are very similar in structure but very different in ac-

tion on the male prostate, and on the male and female breast. Also, estradiol dipropionate and diethyl stilbestrol apparently exercise identical effect upon these tissues so far as observation have been made to date. These observations on the similarity and dissimilarity of tissue reaction should demand that reports presented should be specific in stating that a certain chemical compound was used, rather than androgens or estrogens. These formulæ suggest that the liver plays a most important role in this problem fully comparable to its size.

In the field of tissue culture in experimental research, observations are being made upon the influence of the various endocrines, singly and in combinations.

The volume of contributions on the value of sex hormones, both experimentally and clinically, is too large to go into except to say that most of the observations are to the effect that the estrogenic substances produce an increase in the size of the prostate gland. The following reports are all that could be found which indicated a reduction in the size of the prostate:

Noble[12] reported atrophy of the testicles, seminal vesicles and prostate in male rats due to the administration of diethyl stilbestrol, which he said inhibited the anterior pituitary. Mellish stated that stilbestrol inhibited the growth of gonads in both sexes as well as the seminal vesicles and prostate, that the dipropionate produced greater suppression of the testicles and prostate, and of seminal vesicles, to a lesser degree, than did stilbestrol alone.

Wugmeister[16] reports treating twenty-three male human adults with hyperplasia of the prostate gland with folliculine in large dosages. He gave 100,000 to 200,000 units weekly for twelve weeks. He reported that there was definite improvement in sixteen of the cases as regards the nocturia, the difficulty in urination, and the amount of the residual urine. Nine of the sixteen showed marked diminution of the hypertrophy according to rectal examination or cystoscopy. In four instances the residual remained unchanged but the subjective symptoms were decreased to a considerable extent. There was no untoward disturbance of any kind except the observation of perimalleolar edema and albuminuria in an aged physician, seventy-six years old, who was a definite hepatic. These symptoms disappeared following discontinuance of the injections.

Carrodus and Bolliger[2] reported that their investigations were to

the effect that the prostate was decreased in size in the possum following the injection of estroforme which is the benzoate ester of crystalline ovarian extracts. Incidentally, they also reported that it destroyed spermatorrhea.

Kahle and Maltry[7] reported their observations on the treatment of hyperplasia of the prostate with diethyl stilbestrol and diethyl stilbestrol dipropionate on fourteen patients. They reported a decrease in the size of the hyperplastic prostates in all cases. They also reported striking degenerative histologic changes in the specimens which were excised.

Walter Kearns[8] had an interesting exhibit at the last meeting of the American Medical Association in New York in which he demonstrated that diethyl stilbestrol decreased the size of the hyperplastic dog prostate.

These comprise the only references that I have been able to find that report any decrease in the size of the prostate treated with estrogenic substances. All of the others, of which there are many, and which include Burrows,[1] Deming,[4] Heckel,[6] Zuckerman,[17-24] Van Wagenen[15] and many others too numerous to mention here, report observations to the effect that the prostate gland is increased in size when estrogens are administered.

The substances used are diethyl stilbestrol and estradiol dipropionate. The dosage has been 1 mg. of either given in the deltoid three times a week to once a week and for variable periods.

The first patient was a man, seventy years of age, in poor condition from a vascular standpoint with a history of gradual increase in the frequency and nocturia over a period of some months. Nocturia at that time was ten to twelve times with dribble micturition accompanied by moderate pain. Rectal examination disclosed a mass about three times the usual size of the prostate gland with the right side a little larger than the left, uniformly firm, and immovable. There was no residual. Urinalysis gave negative findings. A roentgenogram of the kidneys, ureters and bladder revealed no bony change. One milligram of estradiol dipropionate was injected into the deltoid. Two days later the patient reported that he got up only four times the night before, that he could void much more easily, and it was a stream instead of a dribble. He felt much better in every way and had much more strength. There was a definite change in the consistency of the gland, it was not so fixed, and the surface was softer. Another milligram of estradiol was given and two days later he reported that he had gotten up twice the night before, that his stream was still fuller, and that he felt normal in every way. The gland was definitely softer.

From this time until a total of nine injections, at the rate of three per week, had been given, he continued normal in all respects. The gland underwent a series of changes of consistency characterized by a softening followed by a firming in both lower poles and appreciable decrease in total bulk. After an interval of two months he was getting up four to five times at night, had a small stream, but was feeling very well. The gland was smaller than when he left with more firmness in the lower poles, and more on the right than on the left. Another series of nine injections resulted in approximately the same response in every respect as before with a nocturia of one to two times and an excellent stream after the conclusion of the injections.

After another interval of two months he returned with a nocturia of four to five times, a smaller stream, and a smaller gland with uniform firm consistency, but not as firm as at first. From that time, March 20, to the present he has been on injections at five-day intervals, with a satisfactory status in every respect. The gland is now as small as it has been, which is about two-thirds of the original size (as accurately as can be estimated). His breasts had been tender, the nipples and areolæ more pronounced, and there was some thickening of the breast tissues. He had increased in weight moderately.

In addition to this patient, six patients have been treated, four with diethyl stilbestrol and two with estradiol dipropionate, with variable response but always improvement. One patient with extensive osseous involvement has been getting relief from pain, as has been the case of pain in all instances where it has been present. No opiate has been necessary for pain when these injections are given and this relief is exceedingly gratifying. A number of benign hyperplastic prostates have been treated with rather satisfactory response and in addition, and as a corollary, two extensive breast carcinoma patients with metastasis have been treated with injections of 25 mgm. of testosterone propionate, with the most prominent response the relief of pain. No tissue studies have been made after these injections, as no glands have been removed, resected, or deaths occurred to make autopsy possible up to the present time. The tissue studies on glands resected before treatment confirmed the diagnosis of malignancy in three instances in which resections were done. Tissue studies on two benign prostates after injections of estradiol dipropionate failed to disclose any findings different from the usual picture of prostatic hyperplasia. One of these microscopic tissue cases was reported by Dr. Oscar B. Hunter and the other by Col. James E. Ash. One autopsy in one of the breast cancer cases has not been reported so far as the tissue is con-

cerned at the present time, but as soon as the tissue studies are completed these reports will be available.

No toxic manifestation has been noted except a little edema in one patient who was feeble and under treatment for hyperplasia. This patient cleared up with reduction of the dose to ½ mg.

The tissue-water balance seems to be influenced to a variable degree. There is definite indication that part of the reduction in the number of times of nocturia is due to a decrease in the total urine output. The pain relief is interesting to speculate upon. With Selye's work it is possible that this may be due to an anesthetic action of these hormones, but in his work little response so far as the production of anesthesia is concerned was noted with estradiol and diethyl stilbestrol. No change could be demonstrated in a roentgenogram of a bony metastatic patient over a period of three months. The change in consistency is very interesting and seems to follow a definite sequence in the patients observed to date. The change in bulk is variable. Dr. Parsons reports a decrease of thirty-three per cent in ten days in one carcinoma case under his observation. The breast changes are most interesting and variable with both substances. Unfortunately, the only patient in whom a large breast mass was formed, which was about 4 cm. in diameter and 1 cm. thick, has not allowed us to remove it to date. This patient was one on diethyl stilbestrol and had a very extensive involvement locally.

An interesting patient who had a total perineal prostatectomy in 1931 by Dr. Gilbert Smith of Boston for carcinoma, had complete retention which necessitated tri-daily catheterization of a malignant mass just anterior to the location of the prostate, which was firm and about 4 cm. in diameter following deep x-ray therapy in November, 1939. Following two weeks' treatment with diethyl stilbestrol he was able to void two to three ounces at a time and catheterized himself only once a day instead of three times. Five days later he reported that he had only two ounces of residual; when I checked his residual in the office it was 10 ounces. On May 16 he stated that he lost a few drops of urine when he coughed. On May 26 he reported he had not catheterized himself for five days. The mass has gotten softer but not small enough to determine any appreciable change in total bulk. His nipples were tender and darker but no masses were felt and he felt better generally. He is now on a weekly injection basis.

CONCLUSION

Estradiol dipropionate and diethyl stilbestrol are substances which seem to relieve pain due to local prostatic malignant tissue and bony metastatic carcinoma. These substances modify the physiology of breast and prostatic tissue in a demonstrable manner. The ultimate result of this action is not predictable at this time and pathologic microscopic studies have not been possible.

Relief of dysuria, nocturia and reduction in residual are pleasing early responses to this form of treatment.

As time goes on it is to be hoped that these observations will serve to stimulate progress in specific tissue control by the administration of these or other yet to be produced substances, realizing full well in the meantime, however, that the complexity of the biochemical problem is such that it may be a long, long time before completely satisfactory tissue control can be an accomplished fact.

* * *

The estradiol dipropionate and testosterone propionate have been made available through the courtesy of the Ciba Company. The diethyl stilbestrol has been contributed by the Winthrop Chemical Company.

REFERENCES

1. Burrows, H.: Carcinoma mammæ occurring in male mouse under continued treatment with oestrin. Am. Jour. Cancer, 24:613-616, 1935.
2. Carrodus, A., and Bolliger, A.: Effect of oestrogenic hormone on the prostate of the marsupial Trichosurus vulpecula. Med. Jour. Australia, 2:633-641, 1939.
3. Charpy, P.: Cholesterol et cancer. Sang, 12:909, 1938.
4. Deming, C. L., Jenkins, R. H., and van Wagenen, G.: The effects of the estrogenic hormone on the urogenital tract of the male macaque monkey, and upon gonorrheal urethritis in man. Trans. Am. Assn. Gen.-Urin. Surg., 29:485-491, 1936.
5. Diener, F.: Die Einwirkungen der Roentgenstrahlen auf den Cholesteringehalt des Blutserums von Krebskranken. Dissertation, Greifswald, 1935.
6. Heckel, U. J.: The influence of testosterone propionate upon benign prostatic hypertrophy and spermatogenesis. Trans. Am. Assn. Gen.-Urin. Surg., 32:237-261, 1939.
7. Kahle, P. J., and Maltry, E.: Treatment of hyperplasia of the prostate with diethyl stilbestrol and diethyl stilbestrol dipropionate. New Orleans Med. & Surg. Jour., 93:121-131, 1940.
8. Kearns, Walter: A.M.A. exhibit 1940.
9. Luden, Georgine: Progress in cancer research. Minn. Med., 5:519-523, 1922.
10. Mattick, W. L., and Reinhard, M. C.: Further studies of effect of radiation on blood cholesterol in malignant disease. Jour. Cancer Research, 14:426-433, 1930.
11. Mellish, C. H., Baer, A. J., and Macias, A. C.: Experiments on biological properties of stilbestrol and stilbestryl dipropionate. Endocrinology, 26:273, 1940.
12. Noble, R. L.: Effect of synthetic estrogenic substances on body-growth and endocrine organs of rat. Lancet, 2:192, 1938.

13. SCAPIER, J.: Cholesterine et cancer. Bull. méd., 3:52-54, 1938.
14. SELYE, H.: Anesthetic effect of steroid hormones. Proc. Soc. Exper. Biol. and Med., 46:116-121, 1941.
15. VAN WAGENEN, G.: Effect of oestrin on urogenital tract of male monkey. Anat. Rec., 63:387-403, 1935.
16. WUGMEISTER, I.: Le traitement de l'hypertrophie de la prostate par doses massives de folliculine. Paris méd., 1:535-536, 1937.
17. ZUCKERMAN, S.: Influence of oestrogens on prostate glands. Nature, Lond., 137:1032, 1936.
18. ZUCKERMAN, S.: Embryological interpretation of changes induced by oestrogens in male reproductive tract. Lancet, 1:135-36, 1936.
19. ZUCKERMAN, S.: Endocrine control of prostate. Proc. Roy. Soc. Med., 29: 1557-1568, 1936.
20. ZUCKERMAN, S.: Effects of prolonged oestrogenic stimulation on the prostate of the rhesus monkey. Jour. Anat., Lond., 72:264-276, 1937-38.
21. ZUCKERMAN, S., and GROOME, J. R.: Etiology of benign enlargement of prostate in dog. Jour. Path. & Bact., 44:113-124, 1937.
22. ZUCKERMAN, S., and PARKES, A. S.: Effect of sex hormones on prostates of monkeys. Lancet, 1:242-247, 1936.
23. ZUCKERMAN, S., and PARKES, A. S.: Effects of oestrone on prostate and uterus masculinus of various species of primate. Jour. Anat., Lond., 70: 323-330, 1936.
24. ZUCKERMAN, S., and SANDYS, O. C.: Further observations on effects of sex hormones on prostate and seminal vesicles of monkeys. Jour. Anat., Lond., 73:597-616, 1938-39.

DISCUSSION

Dr. Clark M. Johnson (San Francisco, Calif.): I disagree with Doctor Bumpus as to the most common site of origin of carcinoma of the prostate. Our opinions as to the proper method of treating patients with early carcinoma in general are so far apart that a brief discussion would be futile. However, he may be right on one point. In rare instances, he and others may have cured carcinoma of the prostate by transurethral resection. I can contribute one instance of such a possibility. A patient was sent to me who had had a transurethral resection for a supposed median bar. Pathologic study of the tissue showed carcinoma. These slides were checked by four independent pathologists, and they all agreed that some of the tissue was malignant.

A radical perineal prostatectomy was done and the gland was carefully sectioned and not a bit of carcinoma was found. It has been three years and there has been no recurrence.

Dr. George G. Smith (Brookline, Mass.): I was tremendously interested in Dr. Herbst's presentation because I did not go to Colorado Springs, and I did not hear, consequently, the work that was presented there on these new drugs in carcinoma of the prostate. Certainly, if they will have anything like the effect on malignant tissue that they seem to have had in reported cases, they will be of tremendous help to all of us in handling these cases. I should be very much interested in trying them out when we get back.

Dr. Bumpus' paper, it seems to me, leaves untouched certain rather fundamental factors in carcinoma of the prostate. We might go back once more to Geraghty's work a good many years ago on the site of location of carcinoma of the prostate, when he found that in 85 per cent of a considerable series of cases studied by him, the growth was primary in the posterior lobe, that is, beneath the floor of the prostatic urethra, a region which I should think even the most skillful resectionist would find difficult to remove with the resectoscope. It is quite possible that malignant tissue in that region would escape detection by this method of biopsy and we are all very familiar with the cases that show no carcinoma in sections removed, in spite of the fact that the examining finger shows

perfectly typical changes in the prostate, when the patient is examined by rectum.

Dr. Bumpus has spoken of the invasion of the perineurial lymphatics. I was interested in working up a series of total prostatectomies to find that the patient who has lived longest, now about twelve years, and has absolutely no sign of recurrence, no pain in the bones, no induration around the bladder base showed marked perineurial invasion.

In the series of some twenty prostates which had been carefully studied pathologically, the question of whether perineurial invasion existed was noted. A number of these patients have lived and done very well. I haven't the figures here so I don't want to make any definite statement about it. They are in a paper which I read in Philadelphia last year.

Dr. Bumpus speaks of the mortality of total perineal prostatectomy. I think the mortality of that operation is, if anything, rather less than the mortality for simple hypertrophy. That seems rather illogical and yet the figures bear that out; this is due to the fact that the cases are selected carefully and one does not attempt to do a total perineal prostatectomy unless the patient is in very good condition and generally not too old.

I still feel that there is a very definite field for total perineal prostatectomy, and I can hardly believe that apparent cure by the method of transurethral resection is anything but a very, very occasional instance.

Dr. J. A. Campbell Colston (Baltimore, Md.): I would like to say a few words about Dr. Bumpus' presentation, and to take issue with his attitude of defeatism on the subject.

Certainly, it seems to me that the radical operation has a definite place, and from our own experiences which correspond exactly with Dr. Smith's, the idea that the mortality of the operation is so much larger than that for the operation for benign hypertrophy, I think, is quite unjustified.

In support of this contention, I might say that for the past four or five years, each one of the residents at the Brady Urological Institute has carried out several of these operations and there has been no mortality.

As our experience with this operation increases, we feel that it should be applied in more and more cases. Dr. Smith was one of

the first to emphasize the excellent palliative results obtained from this operation in cases where it was impossible to remove the entire malignant process, and there could be no hope for a complete eradication of the disease. In such cases, the malignant tissue which is left behind lies in the region of the tips of the seminal vesicles and in that location, with the slow growth of the neoplasm, there is no encroachment on the vesical orifice; hence, no obstruction occurs and the patient, in most instances, has no disturbance of urinary function until death occurs from metastases. This picture is in direct contrast to the progress of a similar case treated transurethrally, when multiple operations are usually necessary, and ulceration and infection are almost inevitable with their accompanying symptoms of frequency, burning, urgency and hematuria.

Furthermore, in addition to the above considerations, when one remembers that the radical operation offers the only possible cure for carcinoma of the prostate, it is difficult to understand why this operation is not more widely used and the results which can be obtained from it better appreciated. Because, with this understanding, I am sure that there would be less of the spirit of defeatism and that the only too prevalent idea that carcinoma of the prostate is a hopeless disease, only to be treated by palliation, would be largely dispelled.

Dr. John B. Wear (Madison, Wisconsin): I'd like to strike a young and immature blow for radical perineal prostatectomy. I certainly disagree with Dr. Bumpus when he talks about the mortality. Up to the present time I have done only a very few cases, somewhere between fifteen and twenty radical perineals. I have been very fortunate. I have not had any mortality with them yet.

But I have been particularly struck by the fact that those who have left the hospital and have come back again for the check-up, by and large, have been much more comfortable than the ones who had very advanced carcinoma and had resections.

Another thing that strikes me as peculiar about our attitude toward carcinoma of the prostate is the defeatism, as it has already been referred to. If we persist in this attitude in carcinoma of the prostate we are never going to make any real, honest effort to cure the patient. The surgeons do not hesitate to do a radical operation on the lower rectum and give the patient a colostomy, but the urol-

ogist has a horror, it seems, for the patient to have an incontinence or to have to wear a bag after doing an operation of this type.

However, all of them don't have to do it, but I expect them to, and then when they don't, that is so much the better. But simply because they may be inconvenienced by a bag if you can possibly cure the cancer, they are certainly no worse off than a man who is wearing a colostomy bag, and that is certainly an accepted operation.

I am going to continue to do the radical operation, and if I live long enough—and I hope my patients will live long enough—in the future I am going to present them before this society.

DR. JOHN K. ORMOND (Detroit, Mich.): Sometimes the statement of a man of small experience has some value. In our clinic we do not do perineal prostatectomies as a routine. Although practically all of our prostatectomies are suprapubic, we have done a few radical prostatectomies for carcinoma. We have done nine without any operative mortality; only one of our patients is incontinent, so we feel that this operation has a distinct place in our armamentarium.

I should like to tell you of another case that shows the resistance of some of these men to carcinoma. In 1928 we made a diagnosis of inoperable carcinoma of the prostate on a man of seventy-three. We did not tell him what the trouble was. In 1932, he came back with retention and had a suprapubic prostatectomy, with removal of hypertrophied lobes, but leaving behind, we knew, a large mass of hard tissue. On section the tissue removed showed carcinoma.

The patient recovered and was well for four years. He returned in 1936 with retention and a resection was performed. Again the tissue showed carcinoma. He returned in 1938 with recurrent retention and another resection was done. He went ahead with his business in perfect health and returned in 1940 for another resection. He now carries on at the age of eighty-six; president of a company that is quoted on the "big Board"; trustee of a large educational institution in the Middle West; very active in business; and a factor to be considered in everything that he undertakes. Unfortunately, since the last resection, he is partially incontinent, but otherwise is in very good shape.

DR. GEORGE R. LIVERMORE (Memphis, Tenn.): Recently two new factors were brought out in the diagnosis of carcinoma of the prostate. I would like to ask whether any of you gentlemen have

had any experience with them. One was an increase in the phosphatase in the blood, and the other was an increase in the sedimentation rate. If anybody knows about these, will you please tell about it?

DR. WILLIAM J. BAKER (Chicago, Ill.): I would like to discuss the clinical application of diethyl stilbestrol. We have been using it since last December and it is remarkable in affording relief from pain to these patients.

I cite the instance of a man of forty-seven, with a large carcinoma of the prostate. We resected him and his chief complaint after that was pain. He received heavy x-ray therapy in several courses. He still complained of pain and we started him on diethyl stilbestrol in heavier doses than Dr. Herbst gave. We gave him a milligram three times a day for two weeks.

I want to warn you about its side effects. Within forty-eight hours, his pain was relieved and the patient felt fine. Within two weeks, his testes had shriveled down to the size of a hazel nut on both sides, and his breasts were large, but he said he would stand for complete castration as long as he felt so well. He put on about 15 pounds of weight in two weeks. We maintain him in his present state at one milligram a day. So, one must warn the patient about the shrinkage of the testes and penis.

DR. ROGER C. GRAVES (Boston, Mass.): I am in complete agreement with Dr. Smith and Dr. Colston and Dr. Wear, and I take issue with Dr. Bumpus concerning his case of carcinoma of the prostate. My experience exactly parallels that of Dr. Smith, as regards the risk and mortality of total extirpation of the prostate for carcinoma. With reference of Dr. Bumpus' argument, it seems to me that to fail to attack a tumor because it may have lymphatic extension, when the evidence of such extension is not clinically demonstrable, is fallacious and would lead us to hold our hands many times when the patient would be benefited by active intervention.

In Dr. Bumpus' case, with the facts as they were first supposed to be, I would agree that the patient should have had, or could have had with advantage, a total perineal extirpation of the prostate. If the patient preferred not to be operated upon or if the surgeon in charge felt that the operation was unwise, excellent palliation could have been given in a case of that type by irradiation, either inter-

stitial, which I prefer and which gives most excellent palliation in our experience, with long control of the disease, or external irradiation, not with any idea of cure, because I believe that cure of carcinoma of the prostate by irradiation alone is an extremely unusual event, but with a view to arrest and control the malignant process and preparation of this area for more successful subsequent resection. I think that many times transurethral resection without irradiation, in the presence of active malignant disease of the prostate, gives a rather unsatisfactory result, first, because of bleeding from the tumor, and second, because of rapid regrowth of obstructive neoplasm within a relatively short time after the operation. When irradiation is given first and an avascular fibrosis is created locally, resection can be done much more satisfactorily, with better immediate results and with, I believe, more lasting benefit. Our form of irradiation under these circumstances consists of interstitial irradiation, with radon seeds implanted into the prostate through the intact perineum, with the guidance of a finger in the rectum, by means of a special applicator which we have made, which permits the introduction of the desired number of seeds, with only two small puncture wounds in the perineal skin.

DR. CLYDE L. DEMING (New Haven, Conn.): May I ask a question? I'd like to ask Dr. Herbst if he feels that the relief of pain from the use of these drugs is due to the analgesia or to the reduction of the fluid in the tissues.

DR. BENJAMIN S. BARRINGER (New York, N. Y.): Whether I agree or disagree with the various methods here used, I am perfectly delighted that our Association has gotten over the very deplorable defeatism in carcinoma of the prostate. I would like to predict that from now on, we may cure a few cases! (*Laughter*)

As a matter of historical record, I'd like to remind you of the first case that ever had a radon seed inserted through the perineum into the prostate. The late Dr. Duane of Boston and I figured for a month or two about the size of the seed. We were using glass seeds at that time. I had a gentleman with a prostate as large as my fist. We decided a sixteen millicurie glass seed could be put in with safety. That is about twenty or thirty times the dose that we use now. He didn't have very much ill effect. He was pretty sick, anyway, but this one seed evacuated a hole in his prostate about as large as a hen's egg. This was done in 1916, I think. (*Laughter*)

DR. H. C. BUMPUS, JR. (Pasadena, Calif.): It is always gratifying to an essayist to have his paper produce a copious discussion even if it is adverse. In closing I desire only to emphasize how prone our profession is to accept the findings of a single investigator as final. Because one pathologist many years ago found cancer to appear more frequently in the posterior lobe in those cases he studied, it has been reported in multiple texts since as usually originating in this location. Yet Kahler, in the several hundred glands he studied, found it more frequently in the lateral than the posterior lobe. Therefore, any theories of treatment based upon the premise that malignancy most frequently originates in the posterior lobe would seem fallacious.

DR. WILLIAM P. HERBST (Washington, D. C.): Dr. Livermore asked about the sedimentation rate. It seems to me that depends pretty much on some of the observation of the various workers on the relationship of stilbestrol and the lipoids of the cell membranes, and the influence of the proportion of those substances in the blood and their effect on the blood cells themselves.

It seems to me that that runs hand in hand with those observations that are now being made in the field of biochemical biology.

I was glad Dr. Baker mentioned the testes because I neglected to state that of the total number of malignant patients, and all of the hyperplastic glands that had been treated, in one patient there has been a decrease in the size of the testicle, and it may be that the difference in dosage that we are using is the answer to that. We shall have to wait and see what the eventual answer is going to be.

In regard to the discrepancy in pathologic pictures, it may be the dosage has something to do with that. For instance, Kahle and Maltry used five or six times the dosage of diethyl stilbestrol that I used in patients and thus explain the inability of Col. Ash to find similar histology.

Dr. Deming asked a question which I am not in a position to answer. Selye wasn't able to produce any degree of anesthesia in animals, utilizing the sterols, diethyl stilbestrol and estradiol dipropionate in moderate dosage in animals. I do not believe it is anesthetic action. It may be due to the disturbance of tissue water balance and there is no question in my mind that the tissue water balance is important in this picture, from another viewpoint, because

the variability in the total urine output has a definite influence, for instance, on nocturia. If a person is putting out only 500 c.c. of urine a night, he isn't going to have to get up as many times as the fellow who is putting out 1,500 to 2,000 c.c.

I do want to emphasize that the effect of these substances on the urinary output is not necessarily uniform, and unfortunately that is one of the difficulties in this biochemical problem, the lack of uniformity in the response of individuals to these steroid hormones.

You see some people who develop breast tumors and others who do not, and yet we inject the same hormone. So the answer is obscure.

THE CLINICO-PATHOLOGIC CLASSIFICATION OF TUMORS OF THE TESTIS IN RELATION TO PROGNOSIS

FRANK HINMAN, M.D., CLARK M. JOHNSON, M.D., and JESSE L. CARR, M.D. (by invitation)

From the Department of Surgery, Division of Urology, University of California Medical School, San Francisco, California

In spite of recent stimuli and renewed interest, there has been little reduction in the mortality of patients with testicular tumor. Radical surgery with removal of regional lymph nodes proved impractical and the more recent promise of cure by irradiation has fallen far short of expectations. The early enthusiasm engendered by the hormonal tests has likewise, in the majority of cases, been of little help in diagnosis and of no avail in materially improving the results of treatment. Furthermore, the pathologic classification of these tumors remains confused and adds little of practical value to the clinician. It seems evident at the moment that only a better clinical awareness and understanding of the whole subject on the part of clinicians, education of the patients, which would result in earlier recognition, together with the advances made in this study, will result in more cures.

Despite this discouraging picture, it seems possible that by continued coöperative clinical, roentgenologic, biologic and pathologic study the mortality may eventually be reduced and the expectancy of life improved. With this incentive and with the coöperation of Dr. Jesse L. Carr (pathologist), Dr. Robert Stone (roentgenologist) and Dr. Herbert Evans (biologist), forty-four patients with testicular tumor have been studied during the past five years. It was our hope that we might find some practical basis upon which to evaluate and correlate the advances which have been made. It seemed particularly desirable to attempt to suggest a pathologic classification of these tumors which would have some relation to their degree of malignancy—their hormonal output, and their response to radiation. If this could be done, some semblance of order could be established out of the present chaotic state. This entire objective has not been accomplished, but a practical and workable clinical pathologic classification has been developed and certain ten-

tative conclusions as to the value of hormonal output and x-ray therapy have been reached.

In order that the results of this study may be evaluated, the plan of treatment followed in all cases is outlined. The method used for the determination of the amount of hormone in the urine and the extent and amount of x-ray therapy used also are presented in some detail.

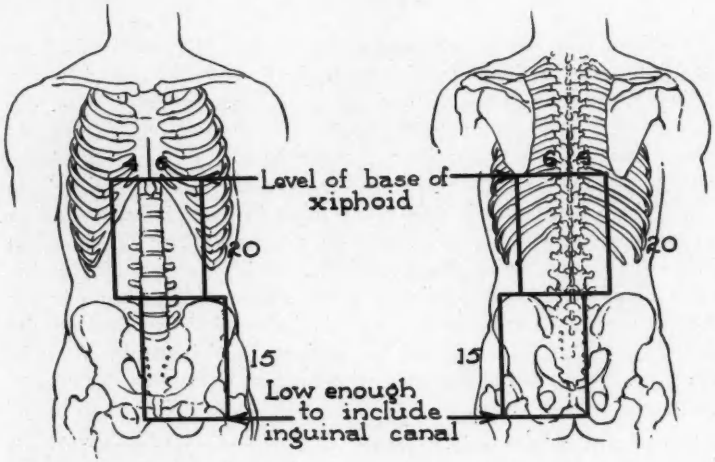

6
Level of base of xiphoid
20
15
Low enough to include inguinal canal
6
20
15
The fields as shown are irradiated. This covers the retroperitoneal lymph channels on the affected side and extends across the midline

Fig. 1.

1. All patients with testicular tumor were subjected to immediate orchidectomy after a collection of a twenty-four hour specimen of urine for quantitative hormonal determination. The operation was done through an inguinal incision, the spermatic cord being clamped and cut with a cautery, followed by extirpation of the testicle.

2. All patients in this series, except two, received postoperative x-ray therapy to the regional lymph zone.

3. Pathologic studies were made of the tissue removed surgically with particular respect to the cytology, complete transections of the tumor being studied rather than any one area. The mutations

and metaplasias of these tumors are of such degree that complete sections of serial character are necessary to reliable cytological diagnosis.

DETERMINATION OF HORMONE

Although the urine of all patients was studied by Dr. Herbert Evans to determine the amount of hormone present, the reports on these tests often were not received before the orchidectomy was

Fig. 2. Embryonal carcinoma with lymphoid stroma, showing a solid field of dark young cells.

performed. This procedure was followed not because of a disregard for the value of the hormonal test in prognosis but because we felt that immediate orchidectomy was indicated in any event and that the presence or absence of hormone was of little value in diagnosis.

Undoubtedly some of the disagreement concerning the value of and necessity for determining the amount of hormone in the urine of patients with testicular tumors has come about because few laboratories are available from which an accurate quantitative de-

termination of the hormonal output can be obtained. Various reliable methods are in use, any of which, using proper animals and properly supervised, is adequate. Each laboratory undoubtedly has its own factor of error. We have been very fortunate in having had

Fig. 3. Embryonal carcinoma with lymph stroma showing a bed of tumor cells and dense stroma of lymphoid character extending up from mature fibrous tissue.

the coöperation of Dr. Herbert Evans, who has checked and rechecked many times the quantitative hormonal output in all of these cases. Below is a brief résumé of the technique used in his laboratory at the University of California.

A twenty-four-hour urine specimen is required. The urine is concentrated by the Levin-Tyndale tannic acid precipitation method (Le-

vin, Tyndale: Proc. Soc. Exp. Biol. and Med., 34:516, 1936) with some slight modification made by Levin.

Two groups of three rats each are used. These animals are normal immature female rats from twenty-five to twenty-six days old.

1. Each rat in the first group is injected subcutaneously, daily for four days, with the amount of powder (concentrate) obtained from one hundred cubic centimeters of native urine. Autopsy is performed

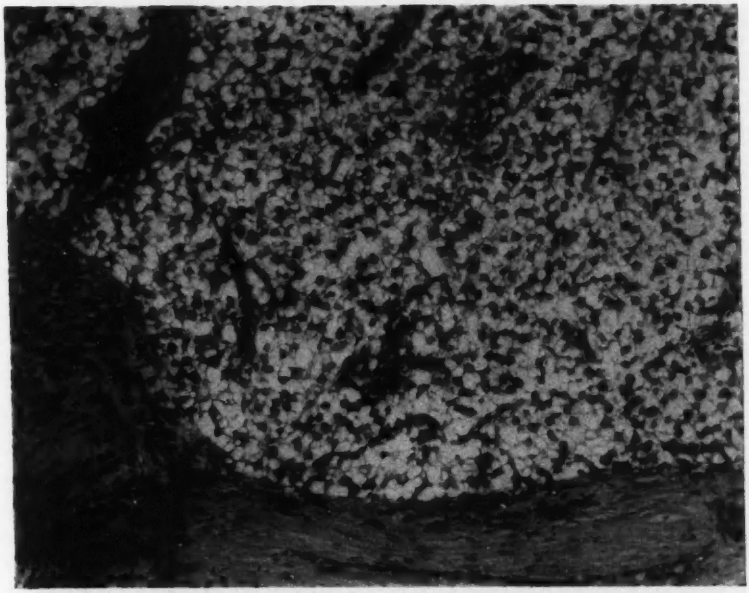


Fig. 4. - Large clear-cell carcinoma showing very fine reticulum, large clear nuclei and a very early lymphoid stroma developing.

on the fifth day. A "positive" test is one showing uterine or follicular stimulation (large follicles, luteinization).

2. The rats in the second group are injected with the concentrate equal to four cubic centimeters of native urine daily over a period of four days.

Results.—If the test is negative in the first group (100 c.c.), there is less than ten rat units per liter.

If the first (100 c.c.) group is positive, and the second (4 c.c.) group is negative, there is between 10 and 250 rat units per liter.

If both are positive, there is over 250 rat units per liter and more urine is then obtained for examination. In these new groups, undiluted

urine and progressively diluted urines are used until a negative test is finally obtained.

X-RAY THERAPY

After orchidectomy all patients were given x-ray therapy to the regional lymph zone. Four fields were treated, as shown in Figure 1, two anterior and two posterior. The size of the field was regu-

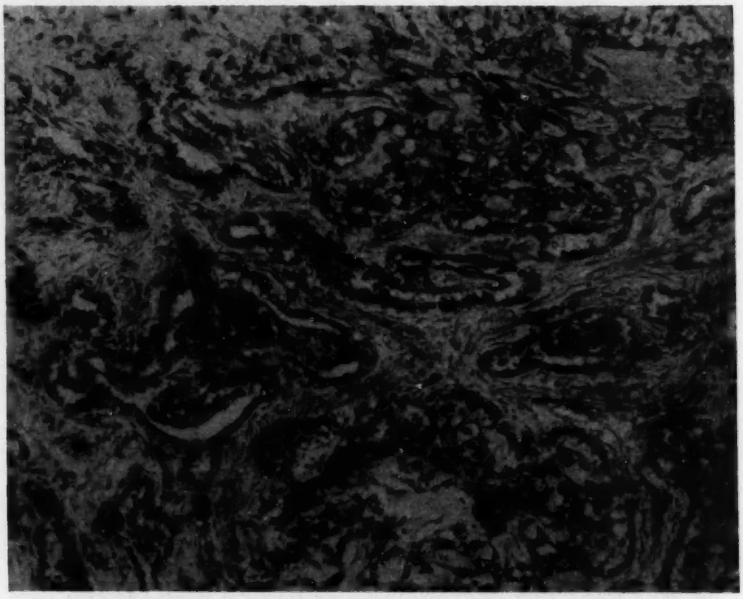


Fig. 5. Adenocarcinoma showing a heavy fibrous supporting structure in which the epithelial cells are forming a papillary and glandular pattern.

lated by the size of the patient and whether or not he had palpable masses. The field always covered the side of the testicular lesion but also covered the midzone and a portion of the contralateral side. Two fields were irradiated each day, preferably treating the same zone anteriorly and posteriorly. The following day the other fields were similarly treated. When a 200 Kv. x-ray was used, 200 r in air was given to each field at each treatment until a total of 2,000 r was received. Most of these patients were treated by the 1,000 Kv. x-ray and in these cases from 250 to 300 r per field was given until

each field had received 3,000 r. Daily doses and total doses varied occasionally, depending upon the patient's reaction to the treatment. Nausea and vomiting, malaise and even diarrhea were the common symptoms. They were never serious and cleared up rapidly when treatment was completed.

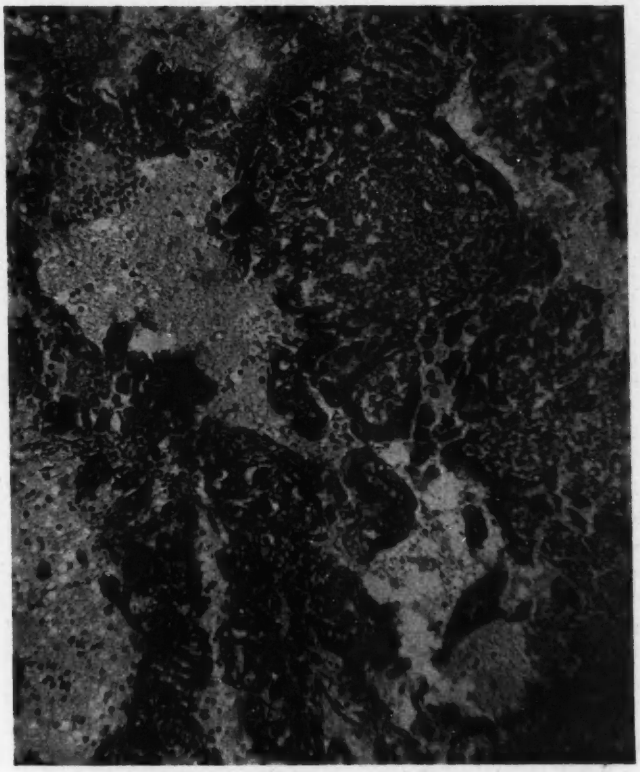


Fig. 6. Chorionepithelioma showing large syncytial cells with areas of necrosis and hemorrhage.

PATHOLOGIC CLASSIFICATION

The pathologic picture of these tumors shows a wide variation in cytologic pattern. The more carefully the subject is studied, the more evident is the conclusion that all of these tumors are related

and that the pathologic picture at any given time represents but a single phase in the development of the tumor. For this reason only a simple clinical classification can be of aid to the clinician. Those who have attempted to be practical and logical have accepted in principle the theory suggested by Ewing* in 1911. When these testicular tumors are seen by the clinician and the pathologist, it is in only one phase—that is, the phase of development reached at that particular time. Only their cell differentiation enables their classification at that moment as to the main pathologic pattern and physiologic function. A sound classification is based upon the cytological grandation of these cells and the pattern they form (Table I).

TABLE I. PATHOLOGIC CLASSIFICATION

	Number of Personal Cases
I. Benign, adult teratoma, dermoid	1
II. Parenchymatous tumors	
(1) Embryonal carcinoma without lymphoid stroma (2) Embryonal carcinoma with lymphoid stroma	21
(3) Large clear cell carcinoma	1
(4) Adenocarcinoma	15
(5) Chorionepithelioma	6
Total	44

1. *Teratoma.*—A teratoma of the testis is a highly differentiated tumor which may show, microscopically, any combination of all possible types of human tissue. Teratomata can be divided into benign and malignant forms only with an understanding of the fact that these tumors, although relatively rare and usually benign, may become malignant. It is only after complete serial section, study of all the sections, and failure to find tissue showing malignant tendency that a good prognosis can be given.

2. *Parenchymatous Tumors.*—These fall clinically into five groups arranged in their relative degree of malignancy, that is, Number 1 is the least malignant and Number 5 the most malignant.

(1) Embryonal carcinoma without lymphoid stroma
(2) Embryonal carcinoma with lymphoid stroma
(3) Large clear-celled carcinoma
(4) Embryonal adenocarcinoma
(5) Chorionepithelioma

*Ewing, James: Teratoma testis and its derivatives, Surg., Gyn. and Obst., 12:230-261, 1911.

Numbers 1 and 2, that is, embryonal carcinoma with or without lymphoid stroma, are the ones previously called "seminoma," a term now discredited. Figures 2 to 6 show typical examples of the cytologic pattern of these five types of parenchymatous tumors.

The theory upon which this classification is based is simply that all of these tumors arise from some totipotent cell which, in any

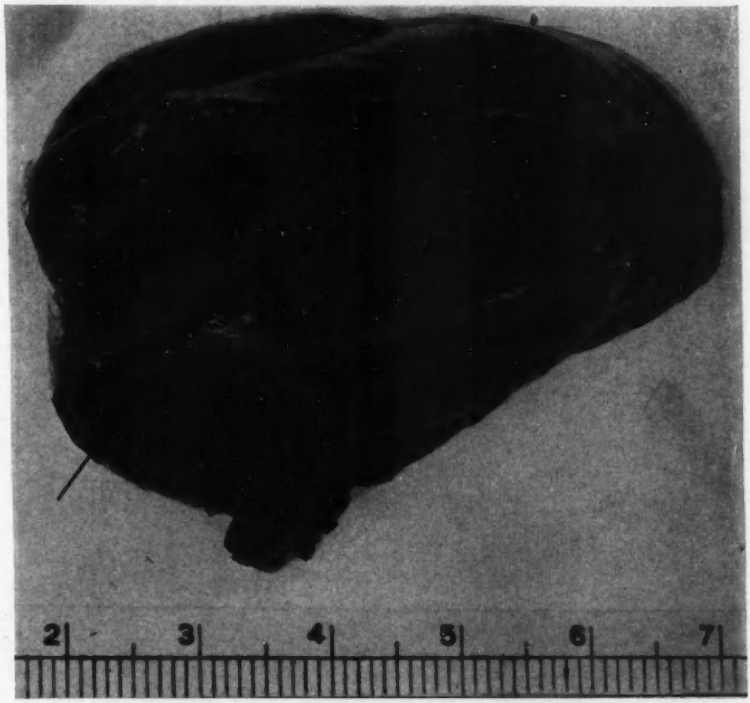


Fig. 7. Gross specimen of right testicle showing small primary lesion (outlined by dotted line).

given person, may differentiate toward the adult or the primitive type of cell. Any combination of cell patterns may be observed in a single tumor. The tumor is classified not according to the predominant pattern but according to the most malignant type of tissue present. Furthermore, it is felt that as these tumors develop or metastasize, they may change their cell pattern completely. The

case history of a recent patient with testicular tumor, on further study, may or may not substantiate this theory.

A boy twenty years of age had been well until two weeks before he presented himself with the following history. His illness began with a cough, hemoptysis and malaise which was considered to be influenza.

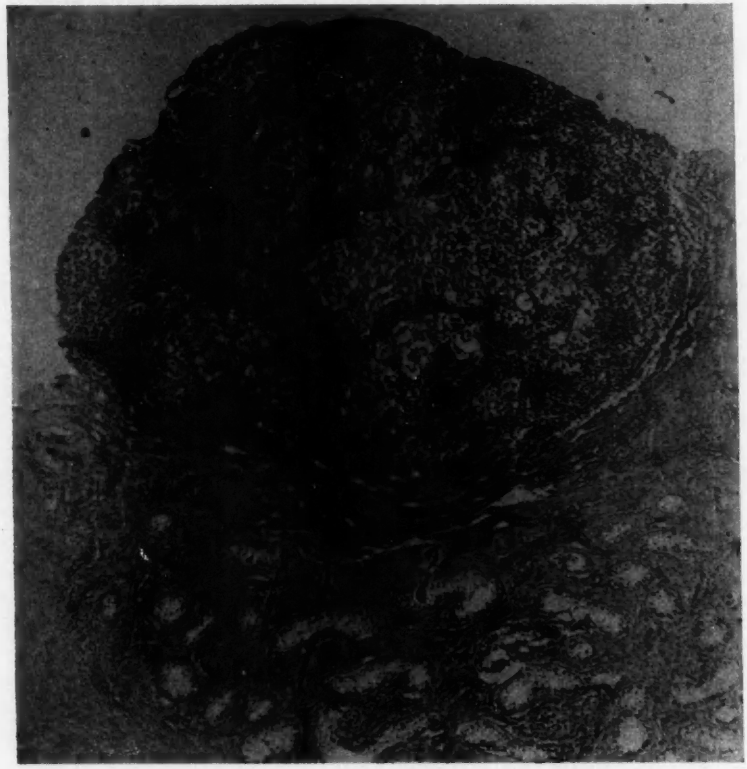


Fig. 8. Embryonal carcinoma with lymphoid stroma showing a low power view of both malignant cells and supporting structure. In spite of the metastatic lesion in this case (Fig. 9), no evidence of chorionepithelioma was found in this original tumor.

After a week in bed, the patient noticed that he had a mass in his abdomen. Examination two weeks after the onset of symptoms showed a well nourished healthy looking young man with a fixed, non-tender mass about 14 cm. in diameter, in the right side of his midabdomen.

X-ray of his chest showed multiple metastases. The character and location of the abdominal lesion together with the appearance of metastases suggested testicular tumor but preliminary examination of both testes was inconclusive. No masses were felt. Cystoscopic examination showed the mass to be retroperitoneal, displacing the ureter medially and causing moderate hydronephrosis on the right side. Careful palpation of the testes finally resulted in the discovery of a small area of induration, not more than a half centimeter in diameter, on the right testis. A clinical diagnosis of chorionepithelioma of the right testicle was made and the urine was sent to the laboratory for hormonal determination. Immediate orchidectomy was done to confirm the diagnosis. The patient was given extensive x-ray therapy to the chest and to the abdominal lesion but continued to fail rapidly and died within three weeks. Autopsy was permitted.

Figure 7 shows the gross specimen and the relative size of the lesion. Figure 8 shows a section through the entire original lesion. Figure 9 shows the character of the pulmonary metastasis which was a typical chorionepithelioma. Section of the original lesion, which was almost microscopic in its total dimensions, though huge metastatic glands were present in the abdomen as well as multiple metastases in the chest, showed embryonal carcinoma with lymphoid stroma. Hormonal determination of the urine showed over 200,000 units, suggestive of chorionepithelioma, which was later proved at autopsy, in the metastasis to the chest. It must be admitted that, although this lesion of the testis was very small, it has not been completely sectioned to date and that perhaps a few chorionepithelioma cells may be found which were not discovered in the original section.

THE VALUE OF HORMONAL STUDIES

Table II shows the hormonal output of the forty-four testicular tumors we have studied carefully. It is readily seen from this table that chorionepithelioma is the high hormone-producing tumor and may be the only one. Another interesting fact is that all fourteen patients in this series who had an increase in the hormone in the urine are now dead. One lived fifteen months, but the average survival after first being seen was only five months. Of the thirty patients without an increase of hormone in the urine, twenty-three are still alive. All forty-four patients received the same treatment, that is, immediate orchidectomy followed by deep x-ray therapy. From this observation, it seems evident that the presence of an abnormal amount of hormone in the urine prognosticates certain and rapid death and that the patient's course is influenced little if any by our present methods of treatment. These studies also con-

TABLE II

Type of Tumor	Rat Units of Gonadotropin per Liter of Urine							Hormone Response	
	Neg.	50	500	1,000	10,000	100,000	1,000,000	Pos.	Neg.
I. Teratoma	Neg.								1
II. Parenchymatous Tumors									
A. Embryonal carcinoma without lymphoid stroma	X		X					5	16
B. Embryonal carcinoma with lymphoid stroma									
C. Large clear cell carcinoma	X			X					1
D. Adenocarcinoma	X				X			3	12
E. Chorionepithelioma						X	X	6	
						Total		14	30

The value of hormone determinations in prognosis:

All 14 patients with increased hormone are dead.

Longest survival ..... 15 months

Average ..... 5 months

Survival of 30 patients with normal hormone: living, 23; dead, 7.

Longest—6 years.

Over 15 months 21

Over 3 years 11

firm the observation that chorionepithelioma always produces gonadotropic hormone, often in great amount.

Correlation of Hormonal Studies and Pathologic Findings.— On the basis of the careful cytologic studies of this group of tumors

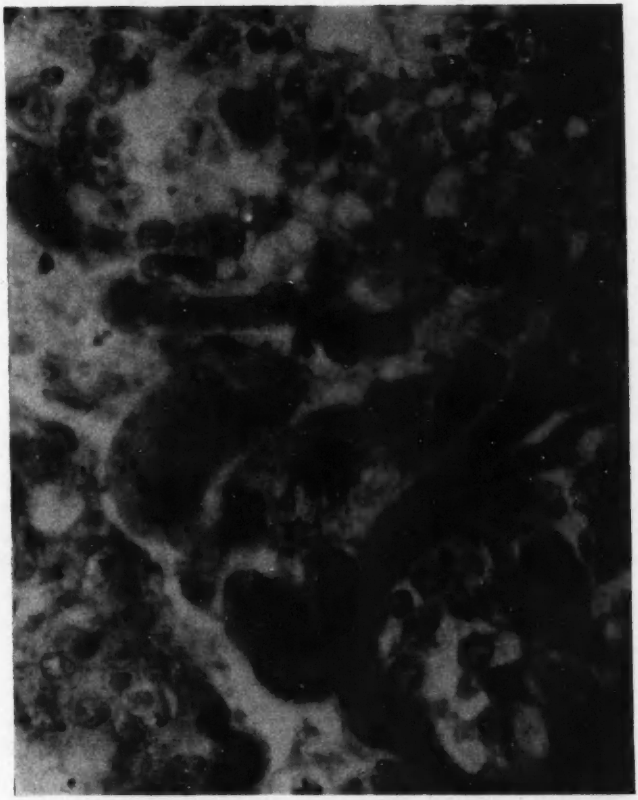


Fig. 9. Chorionepithelioma showing high power view of syncytial cells.

in correlation with the hormonal output, a more definite statement seems justifiable. All patients with testicular tumors who have an abnormal amount of gonadotropic hormone in their urine have

chorionepithelioma. The pathologic proof of the presence of chorionepithelioma may be missing because of inadequate sectioning of the tumor, just as in the case presented in which a complete serial section of the small nodule was not done. A few chorionepithelioma cells may be found on detailed serial section. Only when complete autopsy is performed on a large number of patients with testicular tumor and increased hormone can this statement be substantiated or disproved.

VALUE OF X-RAY THERAPY

It would be unfair to make any statement as to the value of x-ray therapy in general. All patients except two were given the advantage of adequate treatment. Some had demonstrable metastasis when first seen. Others developed demonstrable metastases after x-ray therapy. Some palpable metastases were unaffected by therapy, some decreased in size and some few disappeared clinically. We could not prophesy, after pathologic study of the original testicular lesion, whether or not the metastases would respond to therapy. This was to be expected if our theory is correct that these tumors may develop or differentiate into any type of parenchymatous tumor. In other words, even though a patient has a certain type of tumor cell which should be radiosensitive in the testicle removed and studied, the metastatic lesion may be composed of an entirely different type of cell and be unaffected by therapy. More complete studies which can include autopsies of numerous patients previously studied and treated may permit more definite conclusions.

If any definite statement is justifiable at present, it is that some testicular tumors are radiosensitive, none are radiocurable.

CONCLUSIONS

1. To the best of our present knowledge, all testicular tumors should be treated by immediate orchidectomy, followed by adequate x-ray therapy. Radical removal of the regional lymph zone has been discontinued because careful study of all of our patients throughout the years has shown that not infrequently metastases occur across the midline or even above the surgically available lymph zone before they are demonstrable in the chain of nodes which was formerly removed.

2. The presence of abnormal amounts of hormone in the urine means a bad prognosis.

3. It seems evident that all malignant testicular tumors are so closely related that only a simple clinical classification is justifiable.

4. The malignancy of a given testicular tumor depends upon the degree of the differentiation of cells and this is not constant in any given case.

BILATERAL EMBRYONAL CARCINOMA OF THE TESTICLE

WITH A NOTE ON THE TECHNIQUE OF ORCHIDECTOMY FOR MALIGNANT DISEASE

ROGER C. GRAVES, M.D., F.A.C.S., and
KNOWLES B. LAWRENCE, M.D.
Boston, Massachusetts

From the Urological Clinic of the Pondville State Hospital (Massachusetts Department of Public Health), Walpole, Massachusetts.

In 1853 in the *Bulletin de la Société anatomique de Paris,* M. Bedart described the case of a man of twenty-seven years with bilateral testicular neoplasms. These tumors had been enlarging slowly, one for two years, the other for five months. Denonvilliers performed an aspiration biopsy and obtained "cerebriform" material which was found to be cancer on microscopic examination. An orchidectomy was done on the side of the larger of the two growths. Temporary regression of the other tumor was reported together with improvement in general health. In two months, however, the patient returned with swollen legs and masses in the neck and chest, presumably the result of metastases although there was no postmortem study. We know of no earlier recorded instance of bilateral testicular tumors. It is of interest that the diagnosis was made in this case by aspiration biopsy, a procedure which we regard today as dangerous and without justification in the management of malignant disease of the testicle. In 1887, Theodor Kocher collected from the literature thirteen cases of bilateral "sarcoma" and medullary carcinoma, and added two of his own cases to this list. Many of the published records of bilateral malignancy are not accompanied by pathologic descriptions or the lesions are inaccurately classified. No very satisfactory estimate of the incidence of this condition aside from its obvious rarity, therefore, can be made. In a study of 292 patients with teratoma testis published from the Memorial Hospital in 1935, by Dean, bilateral involvement was not encountered. Lewis and Priestly summarized the literature in 1938, and were able to find only fifty cases of bilateral tumors. They presented two additional cases from the Mayo Clinic. These authors emphasized the strong possibility of error in the total tabulations and in the pathologic classifications of these growths. In the

older reports such present entities as embryonal carcinoma or seminoma were listed frequently as sarcoma.

There are two theories that might be advanced in explanation of the occurrence of bilateral neoplasms. Some authors feel that they

Fig. 1. Photograph of bilateral testicular tumors before operation.

arise independently of each other. Ewing's theory of origin in totipotent sex cells within the testicle would not conflict with such a concept, for of course the opportunities for new growth from such origin are equal on the two sides. A second possibility is that of the metastatic spread of malignant disease from one testicle to the other. The case of a patient with bilateral and unusually large embryonal carcinoma testis constitutes the subject of this report.

CASE REPORT

Pondville Hospital No. 17230. A married Canadian toolmaker, thirty-three years of age, with three children, was admitted May 14, 1940, complaining of swelling of the testicles. Two and one-half years previously he had noted, for the first time, a slight enlargement on the right side. This increased slowly, though with some variations in size, and caused moderate discomfort. Eighteen months before admission, at the time of the first consultation with a physician, the testis had reached the size of a "large egg." Orchidectomy was refused. At about that time the left testicle began to enlarge also. The growth of

both of the tumors continued, the left finally surpassing the right. One month before admission to our clinic, a mass was discovered in the right side of the abdomen. The patient's weight had remained fairly constant, although he complained of loss of strength.

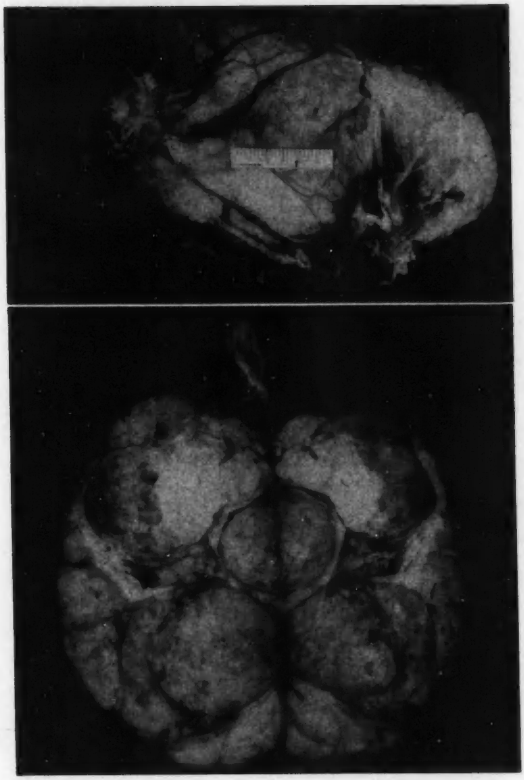


Fig. 2. *(above)* Photograph of tumor of left testicle with attached segment of spermatic cord.
Fig. 3. *(below)* Photograph showing appearance of tumor of left testicle on section.

Physical examination revealed, in the right paramedian region of the abdomen just above the level of the bifurcation of the aorta, a rounded, firm, fixed, slightly tender mass measuring about 3x2 inches. It was apparently retroperitoneal in position. Each side of the scrotum was greatly distended by an ovoid, rounded, smooth tumor, the left

measuring 6 x 4 x 4 inches, the right 4.5 x 3 x 3 inches. These masses were tense and resilient but not hard, and they contained small fluctuant areas. They could not be transilluminated. The scrotal skin was freely movable and the spermatic cords and inguinal regions were nor-

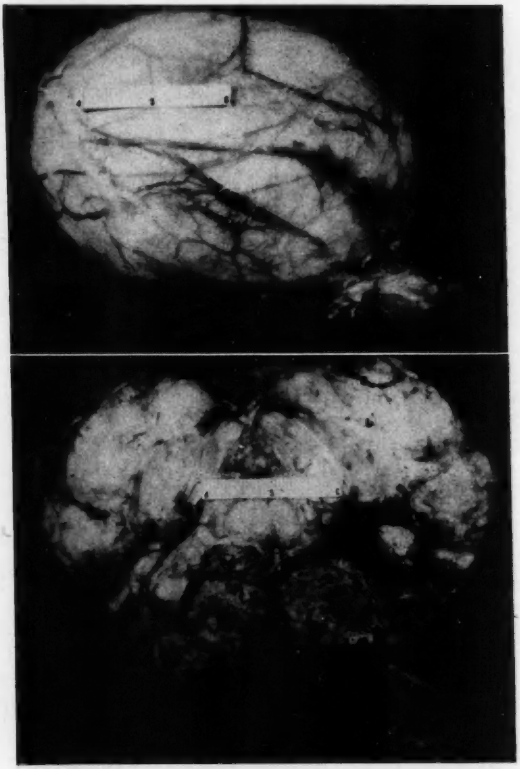


Fig. 4. *(above)* Photograph of tumor of right testicle with attached segment of spermatic cord.
Fig. 5. *(below)* Photograph showing appearance of tumor of right testicle on section.

mal. There was a moderate anemia. The blood Hinton was negative. The white blood count was 4,900, with an essentially normal differential count. The urinalysis was negative. The blood non-protein nitrogen ranged between 24 and 35 mgs. The 'phthalein excretion totalled 60 per cent in two hours. Hormone tests of the urine done shortly after admission and before any treatment was given, revealed an F.S.H.

assay of 80 mouse units per liter. Roentgenograms of the lungs showed no metastases, and the testicular and intra-abdominal masses appeared as soft tissue tumors without calcification.

Left orchidectomy was performed May 29, 1940, especial care being taken to ligate and divide the spermatic cord high in the inguinal canal prior to any manipulation of the testicular tumor. The tunica vaginalis was not opened and was maintained intact throughout the procedure. A right orchidectomy was done in the same fashion one week later. Unfortunately, the weights of these tumors were not included in the record, but as we recall the figures reported at the time in the operating room, one weighed well over 800 grams and the other nearly 900 grams. The total weight of the two together, therefore, was in excess of that of a normal liver. The patient recuperated rather slowly although there were no frank complications.

Pathologic Description (Dr. Shields Warren): The right and left testicular tumors were generally similar in their gross characteristics. The right measured 15 x 13 x 9 cm., the left 17 x 10 x 7 cm., with attached segments of spermatic cord 6 and 9 cm. in length, respectively. The tunica vaginalis was intact in each case and presented on its outer surface fibrous adhesions and numerous engorged vessels. The general consistency of the tumors was spongy. The epididymes were flattened out and not directly invaded. On section the tumors bulged, and oozed sero-sanguinous and mucoid material. The cut surfaces presented numerous soft lobules of varying size and shape separated by gray fibrous bands. Some of these lobules were deep reddish-gray in color, others yellowish or gray and there was gross evidence of liquefaction necrosis. Much of the tissue was hemorrhagic and edematous. The cord structures in both specimens appeared normal. Microscopically no normal testicular structures could be identified. The tissue consisted of sheets and pseudo-alveoli of large polyhedral and rounded cells. The cytoplasm was abundant and clear, the nuclei large and hyperchromatic with prominent nucleoli and occasional mitoses. Foci of lymphoid tissue appeared throughout. The stroma was relatively scanty. *Diagnosis:* Embryonal carcinoma with lymphoid foci, both testicles.

X-ray therapy was begun eight days after the second orchidectomy, and consisted of a series of high-voltage treatments totaling 9,600 roentgen units (air dosage). The factors were 200 k.v., 0.5 mm., copper filter, 50 cm. distance, 200 r per treatment. The treatment was distributed as follows: Right and left anterior and posterior pelvic portals, each measuring 10 x 10 cm., with 1,200 r delivered to each of these portals; right and left anterior and posterior abdominal portals (four) each measuring 10 x 15 cm., 1,200 r. each. All of the area of lymphatic drainage from the pelvis to the diaphragm was covered in this way. The irradiation was tolerated fairly well, with only moderate nausea and anorexia. The mass in the right abdomen gradually decreased in size during the period of therapy. At the time of

the patient's discharge, forty-five days after the initiation of treatment, it was barely palpable.

Two weeks after leaving the hospital the patient returned for observation. The abdominal mass could not be felt. There were no pal-

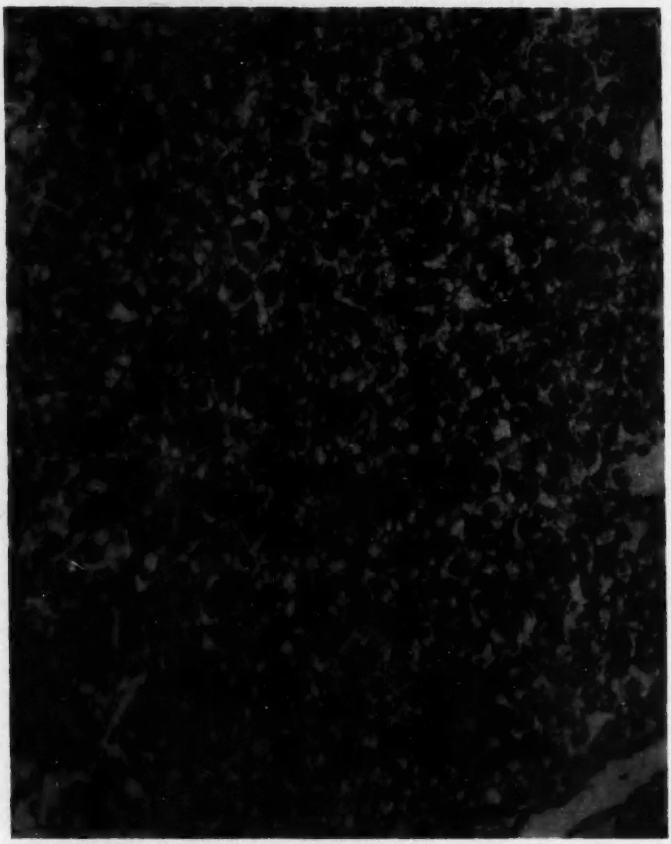


Fig. 6. Photomicrograph of embryonal carcinoma of testicle, with lymphoid foci (× 300).

pable lymph nodes to be found. He had gained 14 pounds in weight and seemed much improved in general health. The urine hormone determination was as follows: "A.P.L. quantitative for teratoma; negative for 8 mouse units per 100 c.c. of urine; negative for 40 mouse units

per 100 c.c. of urine; negative for 100 mouse units per 100 c.c. of urine."

The most recent visit to the clinic was on April 16, 1941. At this time the patient reported that he had lost 5 pounds in weight; he attributed this to the fact that he had had a recent cold. He had no other complaints and was working regularly. On abdominal examination there were no masses felt. The kidney regions were negative. The orchidectomy scars were normal, and there was no evidence of local recurrence of tumor. On rectal examination the prostate was small and soft.

A prolan test of the urine gave the following report: "A.P.L. test, quantitative for teratoma, showed urine precipitated with alcohol and assayed on 6 mice for: 8 mouse units per 100 c.c.; 40 mouse units per 100 c.c. These four mice showed open vaginas, enlarged uteri and enlarged ovaries. No corpora lutea or corpora hemorrhagica seen grossly. 100 mouse units per 100 c.c.; negative. Microscopic: Sections showed evidence of follicular activity but no corpora lutea or corpora hemorrhagica. Conclusion: The test showed a negative A.P.L. reaction, and a positive F.S.H."

This resembles somewhat the report received before operation. We are not yet certain whether it signifies castration effect or the presence of active disease. Dr. Fuller Albright, in whose laboratory at the Massachusetts General Hospital these studies were made, writes: "The test on May 16, 1940, was exactly the same as that on April 22, 1941. Thus, on dilutions of eight units per 100 c.c. and of forty units per 100 c.c. the vaginas of the mice were opened and the ovaries were enlarged and the uteri were enlarged. There was no evidence of corpora hemorrhagica or corpora lutea. These tests can be considered strongly positive for follicle-stimulating hormone and consistent with castration.

"The specimen on August 14, 1940, was entirely negative throughout. It is of interest that this specimen had the lowest specific gravity, namely, 1.016; the specimen of May, 1940, was 1.020 and that on April 22, 1941, 1.030.

"I would conclude, therefore, that the first and third specimens were consistent with what one would expect in castration and that this explained the findings. I cannot account for the findings in the specimen of August, 1940. It should have been positive like the other two. It may be that the patient was somewhat run down and for this reason was producing less hormone. Of course the slight decrease in the concentration of the urine would have made some difference."

In the past at Pondville, we have favored external irradiation rather than surgery as the primary therapy in the treatment of malignant tumors of the testicle, with or without metastases. Orchidectomy is performed in such a program when the full irradiation effect has been obtained in the testicle and when the local re-

action in the scrotum has subsided. In all of our cases, regardless of whether the primary tumor is removed or irradiated, and whether demonstrable metastases are present or not, a full x-ray series is always given and is always understood to include treatment of maximum dosage through both anterior and posterior portals of all the lymph-gland bearing areas *on each side* from the pelvis to the diaphragm. It is dangerous to assume that the spread of disease may take place only on the side of the neoplasm. The strong possibility of metastasis to the opposite side of the body has been well emphasized in the recent excellent paper by Barringer and Earl. We do not treat the chest unless there is x-ray evidence of involvement in this region or unless palpable supraclavicular lymph nodes are present. Under such circumstances the chest and the neck are included in the x-ray program. We believe that surgical dissection of retroperitoneal glands should be reserved for those unusual and desperate cases in which the malignant tumor is of a type resistant to irradiation, as evidenced by its response to treatment or by the pathologic report if the testicle has been removed.

We find now that we are making some exceptions to the rule of irradiation first. In very early tumors with but slight changes to be felt in the involved testicle, and when the presence of neoplasm can be suspected only, a prompt and early diagnosis may not be obtained except by prompt and early orchidectomy. The danger of spreading the disease by this operation, through manipulation or puncture or actual incision of the tumor, is greatly reduced if the operation is properly carried out. We have resorted to surgery first when the tumor was very large. In such cases, x-ray therapy is time consuming; metastases may occur during treatment, since the tumor is subject to constant trauma as the patient moves about; and the amount of irradiation necessary to destroy such a large mass of neoplastic tissue may cause extensive necrosis with the resulting symptoms of toxic absorption. In the unusual case under discussion, moreover, a prompt and correct diagnosis depended upon histologic examination of the growths. That we were dealing with some form of neoplasm seemed quite certain, but of the exact type we could not be sure. We felt that we could exclude without much difficulty such non-neoplastic conditions as hydroceles with thickened walls, and bilateral syphilitic orchitis. Our list of possible diagnoses included: bilateral metastases to the testicles from a

neuroblastoma, which we have seen in two cases, one an elderly man and the other a young boy. While this condition is infrequently encountered it is somewhat more common probably than are bilateral tumors of primary testicular origin. Interstitial cell tumors also had to be considered. An instance of this rare type of growth occurring in both testes simultaneously has been observed by Warren. It might be added that one of two cases of bilateral neoplasms reported by Wollheim was called lymphosarcoma.

Finally, we would like to emphasize the importance of a careful technique for orchidectomy in the presence of malignant disease of the testicle, positive or suspected, in order to minimize the likelihood of widespread dissemination of that disease through undue manipulation of the tumor. No more vicious tumor occurs in the male genito-urinary system and none which is more readily disseminated. We prefer a somewhat more radical procedure than that commonly employed, especially by general surgeons. In all the examinations and preparations for operation, the scrotal contents are treated with the utmost gentleness. The inguinal canal is opened first without including the scrotum in the incision, and high enough to permit adequate exposure of the spermatic cord at the level of the internal inguinal ring. At this level the cord is doubly ligated with as little trauma as possible and without the application of any clamps. It is then divided between the ligatures with the cautery or cutting current. The incision now may be extended downwards sufficiently to permit the removal of the distal cord from its bed and gentle enucleation of the testicle with its intact tunic from the cavity of the scrotum. Great care is taken not to incise the tunica vaginalis or to cut into the tumor at any point. This procedure avoids all manipulation of the malignant process until its lymphatic and vasular connections with the body have been severed.

We describe this simple operation because we are convinced of its importance. Most of the patients with testicular neoplasms that we see have been operated upon elsewhere and the involved testicle has been removed usually through a scrotal incision. Many of them are admitted at Pondville for treatment of the extensive metastases that have developed. These experiences have led us to believe that there is still a general lack of understanding of the ease with which this disease may be disseminated through blood and

lymph channels by too vigorous handling of the tumor at the time of operation. There is too often, moreover, failure to recognize the urgent need of irradiation started immediately after the orchidectomy has been performed and regardless of whether metastatic lesions can be demonstrated or not. Delay until such lesions are obvious will impair very seriously the chances of cure. There has been much argument among urologists as to whether the primary tumor should be treated first by surgery or by x-ray. It is possible that this question would be less important if more attention were directed to the technique of orchidectomy and the roentgen therapy which should promptly follow this procedure.

CONCLUSIONS

An unusual instance of bilateral embryonal carcinoma of the testicle is reported. These tumors were of large size and showed evidence of metastases to retroperitoneal nodes. Preliminary bilateral orchidectomy was done. Clinical disappearance of the metastatic disease followed high-voltage x-ray therapy directed to the abdomen and pelvis. The patient is alive and without definite evidence of disease, about ten months after treatment. The general plan of treatment of testicular tumors is discussed and the technique of orchidectomy is described.

REFERENCES

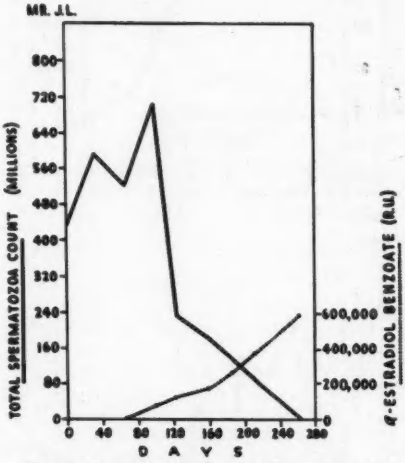
1. ALBRIGHT, FULLER: Personal communication.
2. BARRINGER, B. S., and EARL, D.: Teratoma testis, survey of thirty-seven autopsy records. Surg., Gyn. & Obst., 72:591-600, (March) 1941.
3. BEDART, M.: Bulletin de la Société anatomique de Paris, pp. 345-346, 1853.
4. DEAN, A. L., JR.: Teratoid tumors of the testis. Jour. A.M.A., 105:1965-1971, (Dec. 14) 1935.
5. EWING, JAMES: Neoplastic Diseases. 4th Edition, page 854. Philadelphia: W. B. Saunders Co., 1940.
6. HIGGINS, C. C.: Primary bilateral testicular tumors. Ann. Surg., 88:242-247, (August) 1928.
7. KOCHER, T. (referred to by Dr. Higgins): Die Kronkheiten der männlichen Geschlechtsorgane. Stuttgart, 480-523, 1887.
8. LEWIS, E. B., and PRIESTLY, J. L.: Bilateral testicular neoplasms. Report of two cases. Proc. Staff Meet. Mayo Clinic, 13:737-740, (Nov. 23), 1938.
9. PEIRSON, E. L.: Case of bilateral tumors of testicle with some notes on effect of castration of the adult male. Jour. Urol., 28:353-363, (Sept.) 1932.
10. SMITH, O. C.: Three cases of bilateral tumors in undescended testicles. Boston Med. and Surg. Jour., 170:839, 1914.
11. WARREN, SHIELDS: Personal Communication.
12. WOLLHEIM, J. L.: Bilateral tumors of testicles; two cases. N. Y. State Jour. Med., 30:765-767, (July 1) 1930.

A COMPARATIVE STUDY OF THE EFFECT OF SEX HORMONES UPON THE FUNCTION OF THE HUMAN TESTES*

NORRIS J. HECKEL, M.D.

From Rush Medical College of the University of Chicago, Presbyterian Hospital, and Central Free Dispensary, Chicago, Illinois

In this report a comparison is made between the effects of testosterone propionate and alpha-estradiol benzoate upon the function of the testes.



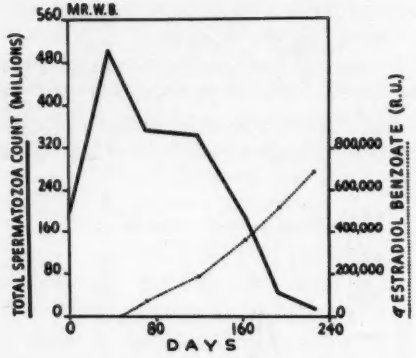
Graph 1. Mr. J. L. Effect of alpha-estradiol benzoate upon the number of spermatozoa.

EFFECT OF MALE AND FEMALE SEX HORMONES UPON THE SPERMATOGENIC FUNCTION OF THE TESTES

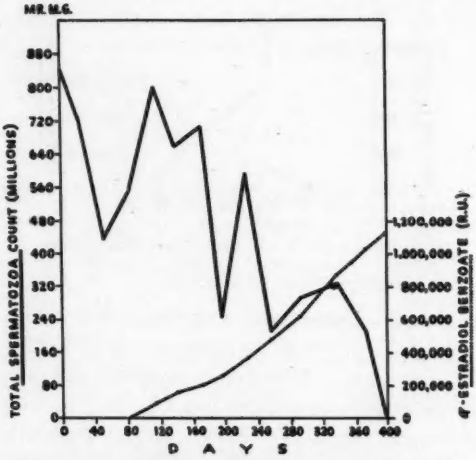
It has been previously shown that testosterone propionate will produce an azoospermia in man,[1,2] likewise in five men who were given alpha-estradiol benzoate either an azoospermia or oligospermia developed. In each of the patients the total number of spermatozoa was within normal limits before the administration

*The Schering Corporation generously supplied the alpha-estradiol benzoate under the trade name of "Progynon-B" and the testosterone propionate under the trade name of "Oreton."

of the hormone. The alpha-estradiol benzoate was given intramuscularly in a dose of 6,000 to 12,000 rat units three to six times a week.



Graph 2. Mr. W. B. Effect of alpha-estradiol benzoate upon the number of spermatozoa.

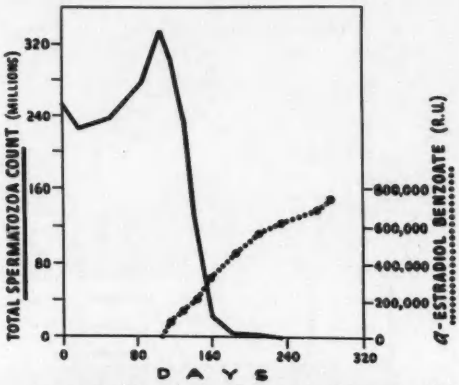


Graph 3. Mr. M. G. Effect of alpha-estradiol benzoate upon the number of spermatozoa.

Case 1.—Mr. J. L., aged seventy-two, has been under observation in the urologic clinic because of symptoms caused by prostatic enlargement. On May 14, 1940, treatment with alpha-estradiol benzoate was

begun and continued for twenty-eight weeks. He received 587,000 rat units of this material. Graph 1 illustrates the effect upon the total number of spermatozoa.

Case 2.—Mr. W. B., aged fifty-eight, was referred to the urologic clinic because of symptoms produced by enlargement of the prostate gland. On November 3, 1940, injections of alpha-estradiol benzoate were started and continued for twenty-six weeks. He received 690,000



Graph 4. Mr. G. S. Effect of alpha-estradiol benzoate upon the number of spermatozoa.

rat units of this material. In Graph 2 is shown the effect of this material upon the total spermatozoa count.

Case 3.—Mr. M. G., aged sixty-nine, was referred to the urologic clinic because of urinary symptoms caused by an enlargement of the prostate gland. On April 20, 1940, injections of alpha-estradiol benzoate were begun and continued for forty-five weeks, at which time he had received 1,114,000 rat units. The effect of this material upon the total number of spermatozoa is illustrated in Graph 3.

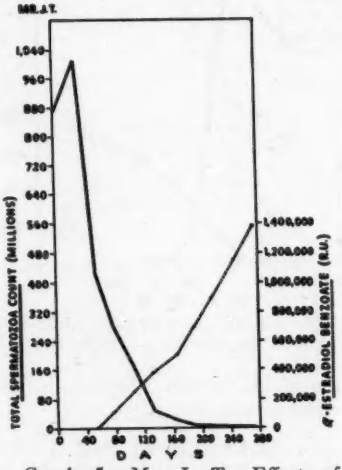
Case 4.—Mr. G. S., aged seventy-two, suffered from symptoms caused by prostatic enlargement. On March 5, 1940, treatment with alpha-estradiol benzoate was started and continued for eighteen and one-half weeks at which time he had received 631,000 rat units of this material. Graph 4 illustrates its effect on the total number of spermatozoa.

Case 5.—Mr. J. T., aged sixty, was referred to the urologic clinic because of symptoms caused by prostatic enlargement. On April 26, 1940, treatment with alpha-estradiol benzoate was started and continued for thirty-one and one-half weeks, at the end of which time he had

received 1,372,000 rat units of this material. Its effect upon the total number of spermatozoa is shown in Graph 5.

HISTOLOGIC CHANGES IN THE TESTES FROM THE ADMINISTRATION OF MALE AND FEMALE SEX HORMONES

Both the male and female sex hormones produce extensive alterations in the seminiferous tubules of the human testes. These changes are characterized principally by atrophy and hydropic degeneration of the spermatogonium cells.



Graph 5. Mr. J. T. Effect of alpha-estradiol benzoate upon the number of spermatozoa.

Case 6.—Mr. F. H., aged sixty. His spermatogenic function, as determined by total spermatozoa counts, averaged 286,936,250 before the administration of testosterone propionate. After he had received 2,430 mgm. of this material in nineteen weeks, his total spermatozoa count had dropped to 16,875,000. At this time a testicular biopsy showed the following: In a section of the testis stained by hematoxylin and eosin, the important alterations are in the seminiferous tubules. There is atrophy and hydropic degeneration of the spermatogonium cells, a few of the tubules have only one layer of cells. But very few of the spermatogonium cells have reached the state of spermatocytes. An occasional spermatid is seen in a few of the tubules, but no spermia (Figs. 1 and 2).

Fig. 1. Photomicrograph of section of testis from F. H. after the administration of 2,430 mgm. of testosterone propionate. Note atrophy and degeneration of the seminiferous tubules.

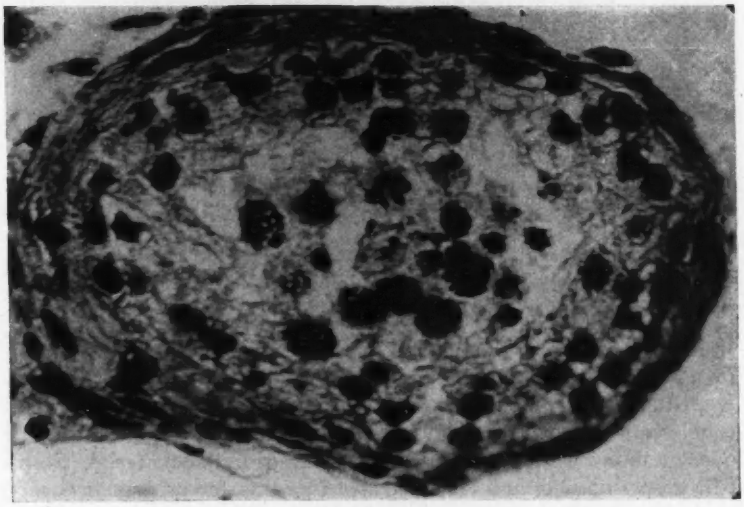


Fig. 2. Photomicrograph of a seminiferous tubule from Figure 1, which shows the arrest in development of the spermatogonium.

In Case 4 a testicular biopsy was made when the patient had received 631,000 rat units of alpha-estradiol benzoate, and his spermatozoa count had dropped to zero. The changes seen in the seminiferous tubules were principally atrophy and hydropic degeneration of the spermatogonium cells with the development of vacuoles. In the majority of the tubules only one or two layers of cells were seen. No spermia were seen. In a few of the tubules the sperma-

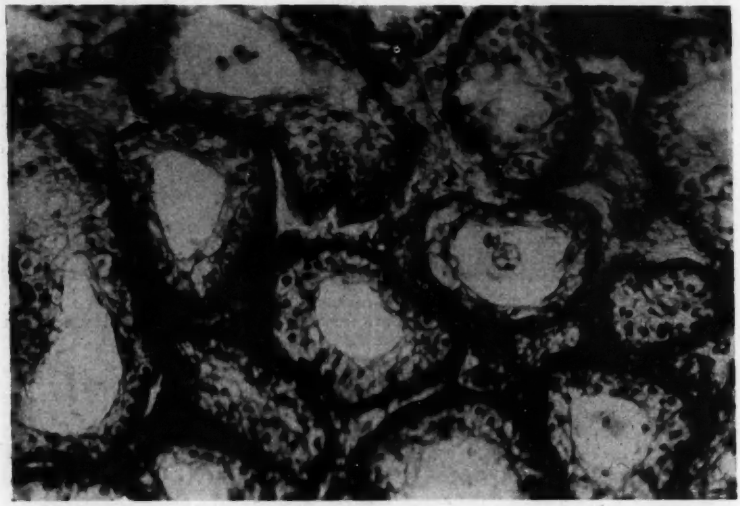


Fig. 3. Photomicrograph of section of testis from Mr. G. S. after the administration of 631,000 rat units of alpha-estradiol benzoate. Note the marked atrophy and degeneration of the seminiferous tubules.

togonium cells had developed as far as primary spermatocytes. However, in a majority of the tubules the arrest of development had occurred before that stage (Fig. 3).

In Case 5 when the patient had received 1,156,000 rat units of alpha-estradiol benzoate and his spermatozoa count had dropped to 2,405,000, a testicular biopsy was made. In the majority of the tubules only one and two layers of cells were present. The centers of the tubules were filled with a fine, pink granular material. Some of the spermatogonium cells had developed as far as primary spermatocytes, but few farther than this stage. No spermia were seen.

The hydropic degeneration was not quite as extensive as seen in the biopsy on G. S. shown in Figure 3 (Fig. 4).

It can be seen, therefore, from a study of the biopsies that both testosterone propionate and alpha-estradiol benzoate produce practically identical changes in the seminiferous tubules. These alterations were primarily a degeneration of the spermatogonium cells. The three biopsies were made at different levels of spermatogenic activity as determined by spermatozoa counts. This can be readily observed in the various stages of development of the cells in the three photomicrographs.

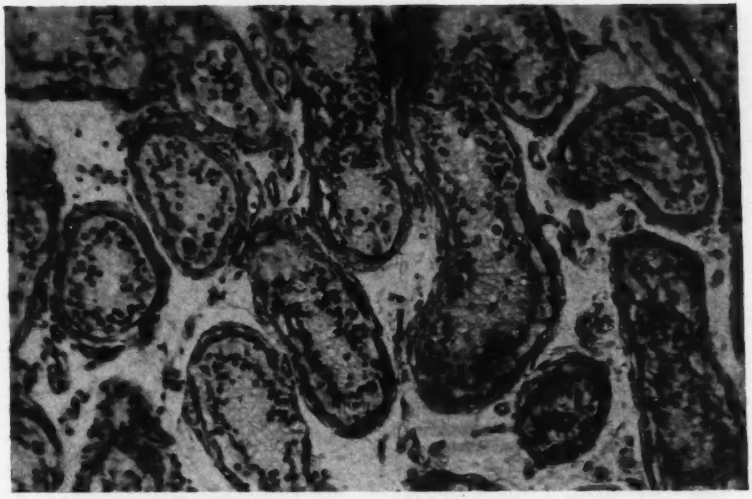


Fig. 4. Photomicrograph of section of testis from Mr. J. T. after the administration of 1,156,000 rat units of alpha-estradiol benzoate. Note the degenerative changes are not as extensive as those in Figure 3.

EFFECT OF MALE AND FEMALE SEX HORMONES UPON THE VOLUME OF SEMINAL FLUID

We have previously shown[8] that testosterone propionate has little or no influence upon the volume of seminal fluid in man. However, in the five patients who received alpha-estradiol benzoate, a striking decrease occurred in the seminal fluid. This is illustrated in Table I, and further amplified in Graphs 6 and 7 for patients J. L. and W. B. taken from the table.

TABLE I. RELATIONSHIP OF VOLUME OF SEMINAL FLUID TO INJECTIONS OF ALPHA-ESTRADIOL BENZOATE IN THE HUMAN MALE

Before treatment		During and after treatment				
		Time specimens obtained			Treatment	
Patient and age	Volume of seminal fluid, c.c.	Volume of seminal fluid, c.c.	After treatment began, days	After treatment stopped, days	Total amount alpha-estradiol benzoate injected, rat units	Number of injections given during period before collection of semen.
G.S. 72	2.9	2.50	11		100,000	10
	2.8	2.20	23		148,000	9
	3.2	2.00	37		210,000	8
	2.5	1.20	57		340,000	13
	2.4	0.80	80		460,000	12
		0.70	105		570,000	14
		0.95	129		631,000	13
		1.10	167		695,000	16
		1.05	182		743,000	8
		1.05		28		
		2.00		73		
		2.70		100		
		3.00		159		
J.T. 60	3.1	1.60	25		120,000	20
	3.65	1.50	54		262,000	25
	2.7	1.00	81		392,000	19
		1.25	112		504,000	17
		0.80	138		712,000	21
		0.75	164		910,000	18
		0.65	194		1,156,000	22
		0.45	221		1,372,000	20
		1.10		49		
		2.80		84		
		3.70		109		
		3.85		139		

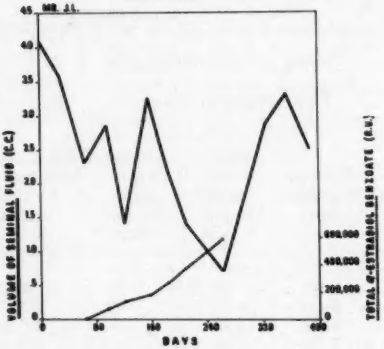
Since this fluid is composed mostly of secretions from the prostate gland and seminal vesicles, it can be assumed that the secretory ability of these two glands is affected by this material. Just how this occurs is a matter of speculation at the present time. Three possible explanations are in order: (1) by direct action of the hormone upon the glands; (2) indirectly through the effect upon the testes, or (3) by depressing the selective activity of the pituitary gland.

TABLE I—(CONTINUED)

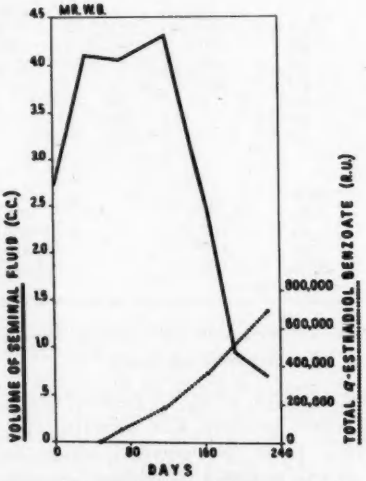
Before treatment		During and after treatment			Treatment	
		Time specimens obtained				
Patient and age	Volume of seminal fluid, c.c.	Volume of seminal fluid, c.c.	After treatment began, days	After treatment stopped, days	Total amount alpha-estradiol benzoate injected, rat units	Number of injections given during period before collection of semen.
M.G. 69	2.4	3.90	32		90,000	15
	3.8	3.60	57		152,000	11
	3.6	4.70	88		197,000	13
	3.2	2.50	114		251,000	9
		4.25	144		359,000	13
		1.45	175		474,000	12
		2.90	209		624,000	15
		3.50	256		862,000	20
		2.25	291		1,018,000	13
		1.35	315		1,114,000	8
		1.60	342		1,246,000	11
		1.55	365		1,354,000	9
J.L. 72	4.1	2.85	32		80,000	14
	3.6	1.40	56		131,000	11
	2.3	3.25	92		179,000	12
		2.20	119		263,000	12
		1.40	145		371,000	11
		0.70	196		587,000	21
		3.00		65		
		3.30		93		
		2.50		128		
W.B. 58	2.7	4.05	24		66,000	11
	4.1	4.30	72		186,000	20
		2.40	117		366,000	19
		0.95	145		510,000	12
		0.70	180		690,000	15

COMPARISON OF THE INFLUENCE OF THESE TWO HORMONES UPON OTHER ORGANS

In the five patients who received alpha-estradiol benzoate, the breasts became enlarged, swollen, and painful; the nipples protruded more prominently from the aerolæ, which took on a deeper brown color. All of the patients developed varying degrees of impotence. These effects have not been observed in similar groups of men who were treated with testosterone proprionate.



Graph 6. Mr. J. L. Effect of alpha-estradiol benzoate upon the volume of the seminal fluid. Note that when the injections of alpha-estradiol benzoate were discontinued the volume of seminal fluid gradually returned to its previous level.



Graph 7. Mr. W. B.: Effect of alpha-estradiol benzoate upon the volume of seminal fluid.

SUMMARY

1. Alpha-estradiol benzoate, like testosterone propionate, produces sterility in man.

2. The degenerative changes in the seminiferous tubules caused by these two hormones are similar.

3. Whereas testosterone proprionate has no effect upon the volume of seminal fluid, alpha-estradiol benzoate produces a spectacular decrease in its volume.

(a) Since the seminal fluid in man is composed mostly of the secretions from the prostate gland and the seminal vesicles, it is deduced that the cause for this decrease in volume is due to the influence of this material upon the secretory mechanism of these two glands.

4. Other untoward effects observed from use of alpha-estradiol benzoate were: hypertrophy of the breasts, enlargement of the nipples, and the development of impotence.

REFERENCES

1. Heckel, Norris J.: Production of oligospermia in a man by the use of testosterone propionate. Proc. Soc. Exper. Biol. & Med., 1939, 40:658.
2. Heckel, Norris J.: The influence of testosterone propionate upon benign prostatic hypertrophy and spermatogenesis: A clinical and pathological study in the human. Jour. Urol., 43:286, 1940.
3. Heckel, Norris J., and Steinmetz, Charles R.: The effect of testosterone propionate upon the seminal fluid in man. Jour. Urol., 45:118, 1941.

DISCUSSION

DR. REED M. NESBIT (Ann Arbor, Mich.): I wish to comment on the subject of testicular tumors and take this opportunity of going on record to state that we have reason to completely disagree with certain conclusions that were published from our Clinic a few years ago regarding a prolan skin test for the detection of prolan in the urine in testicular tumors. The evidence which we have accumulated tends to disagree completely with the report referred to and I believe that it is proper that my opinion regarding the matter be recorded.

DR. DAVID M. DAVID (Philadelphia, Pa.): I'd like to take just a moment to raise one point that I don't think has been mentioned. When I lived in Arizona, I became acquainted with a colleague there who had had a testicular tumor of the seminoma type, I think, removed in Baltimore almost twenty-five years ago now, followed by x-ray treatment. The exact nature and the extent of that x-ray treatment, of course, I do not remember. But suffice it to say that the patient remained perfectly well.

He was a medical student at the time he had this tumor. He graduated in medicine and has been practicing successfully in Arizona for a number of years. He is in excellent health. He is married and has two or three children who, to casual observation, are perfectly healthy physically and normal mentally.

However, in view of the fact that x-ray is given so extensively in these cases and that the remaining testicle cannot escape a good deal of irradiation, I am wondering if we ought not give some thought to the possible production of monstrosities or congenital anomalies in the patients who may survive.

DR. WILLIAM P. HERBST (Washington, D. C.): I'd like to discuss the closing statement of Dr. Heckel's in regard to the possible need for accurate chemical differentiation in the substances that are being used in the treatment of prostatic tissue conditions.

Either I can't agree with Dr. Heckel's observation to the effect that estrogenic substances do not influence the clinical course of hyperplasia of the prostate, or the substance that he is using, while

it isn't greatly different chemically, may be different from the two substances which I described the use of here today.

DR. ROGER C. GRAVES (Boston, Mass.): I have nothing to say, thank you, except to thank Dr. Nesbitt for his reference. I am not sure whether we had it or not, but we will certainly include it.

"THE IMPONDERABLES"

BENJAMIN S. BARRINGER, M.D.
Memorial Hospital, New York City

During the past two years I have seen three patients originally suffering from genito-urinary carcinoma, whom I believed to be dying of the primary carcinoma or its metastases. They looked cachectic, had lost much weight, had grave, unbearable pain and had every appearance of an early demise. All these patients had intraspinal absolute alcohol injections to control their pain.

All three of these patients are comparatively well now. One, I believe, has no malignant disease. The other two are still in the doubtful class as far as final control of their disease is concerned.

The history of these three cases is as follows:

Case 1.—H. L. L., aged sixty-five, was admitted to the Memorial Hospital on October 21, 1940 with a history of having had a bladder carcinoma, which had been treated at another hospital six months before by means of suprapubic implantation of radon seeds. Subsequent to this he was confined to bed. He had lost a large amount of weight. He looked cachectic. The patient was passing some urine through the suprapubic opening and was constantly dribbling the remainder through his urethra. The suprapubic area was widely indurated either from infection or from carcinoma, I could not tell which.

Rectal examination revealed massive periprostatic induration, which likewise was caused by either extensive tumor growth beyond the bladder or inflammation. Under spinal anesthesia cystoscopy was done and the bladder was apparently filled with white slough; with the stone evacuator very large quantities of slough covered with calcareous deposits were removed from the bladder. Subsequent to this the suprapubic wound healed completely. Incontinence ceased, but the patient had a great deal of pain in urinating. On November 20, 1940, an intraspinous alcohol injection of 12 m. was given between the last dorsal and first lumbar vertebra in the right side.* On November 25, 1940, as the first injection had not entirely controlled his pain, a second injection of 14 m. of alcohol was intraspinously injected on the left side. This entirely controlled his pain. He began immediately to improve, got out of bed and went home.

At the present time, May 1, 1941, he has gained about 20 pounds in weight, looks well. His urine is cloudy with pus. He urinates without pain every two or three hours. His periprostatic induration has

*I have used the technique of Elias Lincoln Stearn, M.D. (The American Journal of Surgery, Vol. XXV, No. 2).

almost disappeared. He has had no hematuria and I believe his bladder carcinoma is controlled.

Comment.—This patient obviously was suffering from massive slough formation and infection. Removal of the slough and controlling his pain gave him a chance to get well.

Case 2.—A. F. W., aged twenty-four, was admitted to the Memorial Hospital on November 30, 1937, with the following history: Two months prior to entry he noticed a painless swelling of the left testicle. An Aschheim-Zondek test at the time was negative. The patient was given thirty x-ray treatments to the testicle and the left abdomen. The testicular tumor increased somewhat after these treatments. For three or four days the patient had a dull pain in the left lower quadrant. He had lost about 10 pounds in weight within the past month.

Physical examination revealed a sharp x-ray reaction to the skin on the lower abdomen. The right testicle was atrophic, left testicle the size of a large lemon. Skin of scrotum was desquamating. Aschheim-Zondek was again done and this time showed 500 Prolan A and 100 Prolan B. Later Prolan B increased to 200. There were no masses felt in his abdomen or left supraclavicular region. A roentgenogram of his lungs was not taken at this time.

Hight voltage x-ray therapy was given between December 16, 1937, and January 21, 1938. He received 1,500 r to the left testicle at a distance of 50 cm.; 1,800 r at a distance of 70 cm. was given to each of four portals of entry—left lower abdomen anterior, left lower abdomen posterior, left upper abdomen anterior, left upper abdomen posterior. This had no affect on the size of the testicular tumor.

An orchidectomy was done on February 3, 1938, under spinal anesthesia. The pathologic examination of the tumor removed showed microscopically embryonal adenocarcinoma Grade III. The testicle was partially necrotic but there was much fully viable disease. On April 27, 1938, there was observed a left supraclavicular gland metastasis. A picture of the patient's lungs at this time showed no metastases. His left lower neck and upper mediastinum were given deep x-ray therapy.

On June 28, 1939, he complained of severe pain along the course of the right sacral nerve and was believed to have metastasis here. The right sacral nerve region was treated with deep x-ray therapy with portals anterior and posterior at a distance of 50 cm., 1,200 r anteriorly and 1,200 r posteriorly. This treatment did not affect the pain and the patient began to take codeine. He had lost a good deal of weight and was considered to be in serious condition.

The patient had to have morphine and he finally was taking about ¼ grain every four or five hours. His weight was about 135 pounds. He looked very bad, apparently cachectic and it appeared as if he were soon to succumb from his disease. Because of his pain he was given cobra venom injections and he received twenty-one injections of 1 c.c.

each between February 16, 1939, and March 15, 1939. This gave him some relief but on the whole was ineffective.

The main symptoms were severe pain along the course of the right sacral nerve, general cachexia and great loss of weight. He was given an intraspinous alcohol injection of 12 m. between the last dorsal and first lumbar vertebra. His pain almost immediately disappeared. On June 27, 1939, he reported a gain of some 45 pounds in weight, had no pain, and had returned to work.

On October 26, 1939, he had gained 59 pounds in weight since his lowest ebb; there was some thickness to the left supraclavicular area and he was working.

On August 31, 1940, his condition was excellent, no sign of disease, and he was working.

Comment.—This patient's symptoms were apparently due to pressure upon the left sciatic nerve by tumor which was being changed by deep roentgen therapy into scar tissue. His pain and the sedatives he had to take in the attempt to control the pain gave him every appearance of carcinomatous cachexia. I believe he would have died if his pain had not been controlled.

Case 3.—J. S. was first seen at Memorial Hospital on May 12, 1937, with a history of one and one-half years of profuse hematuria at intervals without pain. On September 1, 1936, a tumor of the bladder was removed in an outside hospital, following which he had some x-ray treatment. Six weeks before admission to the hospital he began to have terminal hematuria with urgency, frequency, pain and nocturia but no incontinence. The patient had lost 30 pounds. Cystoscopy showed a large flat ulcerated tumor, very extensive on the left side of the bladder base and the lower left lateral wall.

The specimen removed showed "epidermoid carcinoma Grade III." The tumor was considered too extensive for a suprapubic implantation of radon seeds. On May 13, 1937, he was treated by a surface application of unscreened radium through the cystoscope, receiving 749 millicurie hours. He had 20 to 30 c.c. residual urine. His condition improved considerably. The radium application caused a good deal of superficial slough of the tumor.

He developed a duodenal ulcer and on May 27, 1938, had a posterior gastro-enterostomy from which he recovered. On September 23, 1938, he had a good deal of bladder pain and dysuria; much slough and calcareous material was washed from his bladder.

On February 21, 1939, rectal examination revealed much induration of the bladder base and he still had an extensive infiltrating tumor. He was put on deep x-ray therapy from February 21, 1939, to April 27, 1939. He received 1,600 r to four portals of entry, left anterior pelvis, left pelvis posterior, right pelvis anterior, right pelvis posterior, at a distance of 70 cm. with a portal of 11 by 14 cm. From June 27,

1939, to July 13, 1939, he received 450 r to four portals at a distance of 50 cm. From August 15, 1939, to September 23, 1939, he received to each of two portals, anterior and posterior, 1000 r at a distance of 50 cm.

On March 7, 1939, he had a great increase of bladder spasm and pain. For this pain between March 10, 1939, and March 22, 1939, he was given ten injections of 1 c.c. each of cobra venom. This did him little good. On March 28, 1939, he entered the hospital and I gave him an intraspinous injection of 12 m. absolute alcohol, the patient living on the left side and injection being between the last lumbar and first dorsal vertebræ. His pain almost immediately stopped. He gained markedly in weight. There was almost complete absence of pain for six months after the alcohol injection.

On December 8, 1939, he was given three blood transfusions 350, 350 and 500 c.c. He still had a moderate amount of hematuria and a recurrence of dysuria, but not enough to indicate another alcohol injection.

On June 28, 1940, the patient was in excellent shape, with some incontinence particularly at night, moderate urinary frequency and lack of sphincter control when he was on his feet. He had gained weight.

On January, 1941, he was free of pain but had urinary frequency. No tumor could be detected through the cystoscope. He had several areas of white slough in the bladder.

Comment.—This patient apparently was dying from his carcinoma during the course of treatment by radiation therapy. Alleviation of his pain turned the tables and gave the radiation therapy a chance to complete its control.

These three cases are in the class of imponderables in genitourinary carcinoma. With just a shade of casualness in estimating the real underlying cause of their condition, with the usual methods of combating their pain, morphine, et cetera, all three might easily have died, not of their carcinoma but of attendant complications.

Without the pain control caused by the intraspinous alcohol injections, two of the patients, I believe, would surely have died.

The explanation of the recovery of the first patient is comparatively simple. He had massive slough and stone formation of his bladder caused by radium implants. These caused severe infection of his urinary tract. Removing the stones from his bladder controlled the infection.

The explanation of the recovery of the two other patients is not as simple. The patient with teratoma testis must have had perineural metastasis as a cause of his pain. His pain alone was causing his physical deterioration and I believe would surely have

caused his death. His subsequent rapid recovery when his pain ceased, his all-around physical improvement gave the roentgen therapy, which he previously had, a chance to complete its ultimate destruction of the metastatic teratoma.

This, perhaps, implicates a new and previously unsuspected principle in the treatment of intractable and extensive carcinoma.

Deep x-ray therapy has proved to be singularly inadequate in controlling many body cancers. This in spite of the persistent endeavors of the best cancer-minded physicians of the entire world. It has been so nearly adequate and yet it has failed.

I think everyone agrees that the obliterating endarteritis in the tumor vessels caused by deep x-ray treatment is a much more important effect than the primary and early cell destruction. The former, however, is a long distance effect. It takes a long time—months, even years.

In most cases the race between the growth of the cancer and the healing x-ray has been a very unequal one. The cancer has nearly always won out. In addition to the cancer growth *per se* causing bodily destruction and finally death, we have long known that infection of the cancer and of organs adjacent to the cancer very materially adds to the bodily disintegration. This is especially true in some internal cancers, *e.g.*, bladder and cervical cancers. In these two the destructive effect of the infection may catch up with and pass that of the original cancer.

To this destructive effect of *infection* must be added, in at least some cases, the destructive effect of *pain*. This is clearly shown in Case 2 and Case 3 above reported. The control of pain releases this destructive effect and certainly gives the deep x-ray therapy a longer and more propitious chance to get in its work.

I believe that more such cases exist than we have ever suspected. The fact that two patients out of fourteen, all considered hopelessly ill of cancer, have become well because of pain control emphasizes this point.

The study of the control of pain in cancer cases may cause even revolutionary changes in the treatment of such cases.

THE USE OF PROSTIGMINE IN THE MANAGEMENT OF POSTOPERATIVE URINARY RETENTION

REED M. NESBIT, M.D., and ROBERT H. CUMMINGS, M.D.
From the Department of Surgery, University of Michigan, Ann Arbor, Michigan

Urinary retention following major surgical operations constitutes a frequent and sometimes serious complication of these procedures. Many of these retentions are entirely functional or reflex since they regularly occur in patients who are free from organic disease of the urinary tract. A satisfactory neurophysiologic explanation of this phenomenon has not been presented, although most observers believe it to be an atony of the detrusor resulting from reflex imbalance of the autonomic nervous system. In this respect it is considered analagous to the complication called paralytic ileus.

Efforts have been made to prevent as well as combat postoperative ileus and bladder atony by parasympathetic stimulation. Various drugs are known to have this pharmacologic action. There are three main groups of these parasympathomimetic agents: (1) the choline esters—acetylcholine, acetyl-beta-methylcholine (mecholyl), and carbaminoylcholine (Doryl); (2) the inhibitors of cholinesterase—physostigmine (eserine) and prostigmine; and (3) the older alkaloids pilocarpine, arecoline and muscarine.

Although the choline esters have been demonstrated to have a favorable effect on ileus and postoperative atony, their widespread use has been discouraged by the toxic manifestations that occasionally are encountered. Patients show highly variable susceptibility to this group of drugs and it has been suggested that in postoperatives this unknown factor of susceptibility constitutes an undesired hazard.

Of the second group of drugs prostigmine has been recommended because of its low toxicity and because of alleged proved value.

Gordon recently reported a series of eighty-five cases in which prostigmine was used. Fifty of these received prophylactic dosages pre-operatively and postoperatively, being given 1 c.c. of 1:4000 solution at intervals of two hours for six doses. Only two patients of this group required catheterization. This 4 per cent incidence of atony was compared to an 18.5 per cent incidence of catheterization observed in a control series of 318 cases. Marden and Wil-

liamson reported a series of 247 cases given prostigmine. Ninety-eight of their cases were given prophylactic doses of prostigmine with a 5.1 per cent incidence of postoperative catheterization. They did not present control statistics.

We have made observations upon a small series of cases in the University Hospital in an effort to determine the usefulness of prostigmine in preventing urinary retention. Simple appendectomies, herniorrhaphies and anal operations were selected as an ideal group for this study. A control series of 285 cases showed a 17.5 per cent incidence of postoperative catheterization. This incidence of retentions approximated the 18.5 per cent reported in the control series of Gordon.

Prostigmine was given in sixty-five cases. The drug was used in two different ways—as a prophylaxis against and as a therapeutic agent in the treatment of postoperative urinary retention.

Prophylactic administration was given as recommended by Marden and Williamson. One c.c. of prostigmine methylsulfate 1:2000 was given at 6 p.m. the night before operation, repeated at midnight and at 6 a.m. the morning of operation. Beginning at four hours postoperative 1 c.c. was given and repeated at six-hour intervals. If the patient developed discomfort and failed to void after twelve hours then 1 c.c. doses were given at one-hour intervals. This failing, the patient was catheterized within eighteen hours postoperatively. Fifty-two cases were treated according to this plan. Forty-five were given pre-operative and postoperative prophylactic dosages as described, and seven were given only the postoperative prophylactic dosage. Our original plan of investigation called for a study of 300 cases in order to eliminate, as much as possible, statistical errors which might occur in a small series. However, since the cost of the drug under investigation is rather high (75 cents per ampule dose, with an average total cost per patient of $4.05) it was decided to tabulate our results after fifty cases had accumulated, in order to determine the trend of results and decide whether continued investigation appeared economically justified. The fact that this study was not subsidized by any outside source but was supported by our patients, who were allegedly deriving benefits, appeared to justify our premature appraisal.

The results are tabulated and compared with controls as shown in Table I.

It is apparent that the incidence of catheterization was not materially influenced by prophylactic use of prostigmine in this group of fifty-two patients. We realize that a numerically small series such as this may well lead to deceptive conclusions. The series reported by Gordon consisted of fifty cases with only 4 per cent of retentions. Marden and Williamson observed a 5.2 per cent incidence of retention requiring catheterization in 247 cases which

TABLE I. PRE-OPERATIVE AND POSTOPERATIVE PROPHYLACTIC USE OF PROSTIGMINE

	Controls			Treated Group		
	No. Cases	No. Catheterized	Per Cent	No. Cases	No. Catheterized	Per Cent
Appendectomy	93	16	17.2	18	3	16.6
Herniorrhaphy	100	22	22.0	31	4	12.9
Anal operations	92	12	13.0	3	0	0.0
Totals	285	50	17.5	52	7	13.6

they reported. The trend in our series did not appear to clearly suggest the usefulness of the drug, so our investigations with it have been discontinued.

Prostigmine used as a therapeutic agent in cases of impending retention was given in thirteen cases. These patients were given 1 c.c. of 1:2000 prostigmine each hour for four doses or until the patient voided. Three of the patients so treated (23 per cent) required catheterization. The remaining ten patients voided spontaneously. It is, of course, impossible to know how many of this particular group would have required catheterization had the drug not been used. All were uncomfortable and apparently in danger of imminent retention when the drug therapy was instituted. Although the realistic or cynical physician might well contend that ten out of thirteen such patients could be induced to void by other means short of catheterization, we feel that the evidence presented tends to credit the drug with some degree of usefulness in treatment of impending retentions.

In conclusion, much has been claimed for the use of prostigmine in prevention as well as treatment of postoperative urinary retention. In some clinics the reported incidence of postoperative catheterization has been reduced to as low as 4 per cent.

In our clinic a carefully controlled small series in which prostigmine was given failed to demonstrate the virtue of this drug in materially reducing the expected incidence of catheterization following simple appendectomy, herniorrhaphy and anal operations.

REFERENCES

1. Gordon, E. S.: Urinary bladder atony complicating the postoperative course of surgical patients, Urol. and Cut. Rev., 44:115, (Feb.) 1940.
2. Marden, P. A., and Williamson, E. G.: The use of prostigmine methylsulfate in the prevention of postoperative intestinal atony and urinary bladder retention, Surg., Gyn., and Obst., 69:61, (July) 1939.

AN UNUSUAL CASE OF PROSTATIC ABSCESS

H. G. HAMER, M.D., and WM. NILES WISHARD, JR., M.D.
Indianapolis, Indiana

Prostatitis of nonspecific origin is of moderately frequent occurrence and, according to Herman,[1] is relatively more often followed by abscess than the specific variety.

The clinical features of prostatic abscess are identical regardless of the source of infection (whether nonspecific or gonorrheal) as are also the clinical features of acute prostatitis and prostatic abscess. In the early stages of the acute infection it is difficult to predict whether the condition will run a benign course and resolve, or terminate in abscess formation.

Careful observation and frequent rectal palpation will aid in the differentiation. The most reliable evidence of abscess formation in the swollen gland is fluctuation. Absence of fluctuation does not exclude abscess. Schwartz[4] and Herman and Carp[2] stress this point. In the submucous type or centrally located abscess the distance from the examining finger may cause uncertainty as to fluctuation. Instances of undiagnosed abscess of the prostate have been recorded in which the abscess was discovered at operation for hypertrophy of the prostate.

Generally recognized as benign, a prostate abscess may terminate unfavorably, if unrecognized and improperly treated. Morton[3] quotes Segond's statistics of 114 cases in which there were thirty-four deaths. Spontaneous resolution is unusual. Recovery generally depends upon either spontaneous rupture into the rectum or the urethra or surgical drainage.

The fatal termination of an undiagnosed prostatic abscess seemed to us sufficient reason for reporting the case.

This man, aged sixty-four, who had previously enjoyed good health, was admitted to the Methodist Hospital on October 30, 1940, and the hospital record shows the following notes:

"Patient was here in September, 1938, because of diarrhea, abdominal cramps and pyuria. Urological examination showed slight enlargement of the prostate, the left lobe somewhat larger than the right, chronic prostatitis and a normal upper urinary tract. The condition was regarded as prostatitis associated with early hypertrophy. Since then he has had occasional rounds of prostatic massage and chemo-

therapy. One week ago, prostatic massage was given in the morning. That evening he had a chill and fever of 101. He has had a variable fever ever since."

At the time of admission to the hospital, urine No. 2 was free from pus. Rectal palpation detected a tense left lobe and normal right lobe of the prostate. The urine voided after massage of the prostate was loaded with pus cells. Urination was not frequent, difficult or painful and there was no pain in the perineum or rectum. Abdominal palpation disclosed no abdominal masses, muscle spasm or tenderness, and no costovertebral tenderness. The external genitalia were normal. The temperature was 98 at 11:00 a.m., 99 at 1:00 p.m., and 103 at 4:00 p.m. The blood pressure was 130/70. The blood count showed: hemoglobin 78; red blood cells 4,080,000; white blood cells 9,600; polynuclears 77; and the phthalein elimination test showed 40 per cent the first hour and 12 per cent the second hour, with 52 per cent for the two-hour period. On November 2, 1940, the hospital notes record:

"The fever continues with daily rise to 102. The patient is nervous and talkative. The heart seems normal. Blood pressure 130/70. Lungs clear. Blood stains for malaria negative.

"November 3, 1940. The fever persists, rectal palpation detects no evidence of fluctuation in the prostate. No cause for fever was found outside the urinary tract. Urine showed x to 2x pus. No bladder symptoms, no pain except slight pain in chest last night.

"November 4, 1940. There was no evidence of urethral discharge upon massage of the prostate. Urine voided after massage was not very cloudy. The prostate was not tender. X-rays showed cardiac enlargement and arteriosclerotic dilatation of aorta, also bilateral basal pneumonitis. Urine culture showed Gram-positive cocci singly and in groups. Examination of the lung fields show one small area of dullness in the right lower lobe and a few moist and crepitant râles, this probably embolic. At 9:00 p.m.—patient perspiring profusely, is much weaker but temperature is lower. Chest examination reveals the same findings and in addition, a pleuropericardial friction along the outer border of the heart and lower one-third of cardiac area.

"November 5, 1940. Blood pressure 112/66. Chest examination—very little pericardial friction heard this morning but there is a pleurisy over the whole of the left lower lobe. The lung findings on the right are about the same as yesterday. Laboratory report—agglutination with B. meletensis and Br. abortus is negative. Widal is negative with B. typhosis, Para A and Para B.

"November 6, 1940. Urine culture—organisms present morphologically and culturally resembling Staphylococcus aureus. Blood culture—no growth. Blood count—hemoglobin 68 per cent; red blood cells 3,270,000; white blood cells 9,600; polynuclears 78. Urine—cloudy, acid, specific gravity 1,030; albumin a trace, sugar negative, urea 1.6 per cent, pus cells many.

"November 7, 1940. Still has mild pericardial friction. There are moist râles at the right base, friction at right axilla and lower lobe. General condition not so good. Heart tones are more snappy. Cardiac area enlarged to left. X-ray—heart slightly larger. Bilateral pulmonary congestion or basal pneumonitis. Blood culture negative. White blood count 17,600; polynuclears 85.

November 8, 1940. Blood culture negative; blood count—white blood cells 17,799; polynuclears 92.

"November 9, 1940. Blood culture negative. Blood count—hemoglobin 62 per cent; red blood cells 3,100,000; white blood cells 16,600; polynuclears, 92.

November 11, 1940. A.M.—Lung fields have not changed since yesterday. Coarse râles heard over left chest, *i. e.*, midaxillary line, 7th to 9th ribs. The heart tones are good, pulse rate 112. Respiration is labored. There is very little cyanosis of the tongue, lips and about the head, indicating some obstruction to venous return from the head. Blood transfusion of 600 c.c. was given. P.M.—General condition decidedly worse. More cyanosis. Poorer aeration on right side, more air hunger. Heart tones not so good. N.P.N.—39.5 mgs. Blood count—hemoglobin 58 per cent; red blood cells 2,850,000; white blood cells 13,600; polys 95.

"November 12, 1940—5:00 a.m.—R.H.C. Cause of death—acute pericarditis, pulmonary infarction, prostatitis and prostatic abscess."

Summary.—A white married man, aged sixty-four, who had been a patient of ours during a period of over two years because of a low grade nonspecific prostatitis, returned after a vacation complaining of cloudy urine which sulfanilamide would not clear up, and a little bladder irritability. Massage of the prostate yielded the usual secretion containing 50 pus cells, more or less, per high power field. The prostate was estimated to be size I benign hypertrophy, of usual texture, and no local tenderness. There was no residual urine. Following a very gentle massage of the prostate the patient had a chill. He returned in a week saying he had the "flu." We put him in the hospital, called an internist who found nothing in the chest at first, and had our digital examination confirmed by our two associates. Inflammatory enlargement of the left lobe of the prostate was noted but no evidence of fluctuation was found. Each rectal examination was followed by chills and fever. Sulfonamides improved the picture not at all. Within another week signs of cardiac enlargement appeared, shortly to be followed by congestive failure and terminal pneumonia within eighteen days of the onset. Autopsy showed (1) a prostate very slightly larger than normal, in whose left lobe was a completely sealed-off abscess 5 mm. in diameter,

smears from which abscess showed Gram-positive cocci, (2) small thrombosed veins and many lymphatic glands along the course of the great vessels, clear up to the mediastinum, (3) acute fibrinous pericarditis, and (4) an incidental aneurysm of the aortic arch.

In retrospect, we believe we would probably again fail to diagnose this abscess if confronted by the same problem, because of our previous familiarity with the prostate in question and its failure to change in size or texture when the abscess developed. The chills made us suspicious, as did also the leukocytosis, but the local findings and the development of serious complications did not seem to warrant but rather to exclude an exploration.

REFERENCES

1. Herman, Leon: Practice of Urology. Philadelphia: W. B. Saunders & Co., 1938.
2. Herman, L. and Carp, J.: Ann. Surg., 81:1115, 1925.
3. Morton, Henry H.: Genito-Urinary Diseases and Syphilis.
4. Schwartz, J.: Jour. Urol., 43:112, 1940.

PRIMARY CARCINOMA OF THE MALE URETHRA

WM. NILES WISHARD, JR., M.D.

From the Department of Urology, Indiana University School of Medicine, Indianapolis, Indiana

From 1862, when Hutchinson[8] published the first authentic report of primary carcinoma of the male urethra, until the fall of 1939, approximately 130 papers appeared dealing with the disease in about twenty more than that number of patients. Many of these papers were in fundamental accord on a number of points: the rarity of the disease, the frequency with which it was found associated with stricture in patients who had had gonorrhea, the poor prognosis when the lesion was located in the posterior urethra, and the basic principles of treatment. Many authors made a brief survey of the literature, adding a case report of their own to the total number of instances reported by the last previous writer.

In 1932, Kirwin[9] challenged the diagnosis in some instances, reduced the total number at that time; and in particular observed that every writer up to 1932, in translating the original French paper, quoted it as cancer of the urethra. He promptly eliminated it. In a personal communication in 1938 he admonished the author not to fall into the same trap.

In 1939, Kreutzmann and Colloff[10] published a paper on the subject which will stand as the definitive statement up to that time. Unlike other authors they went to the original report of *each* previous paper, abstracting it and publishing a table of the findings to that date. It is to be observed that nine of the cases were either not substantiated by biopsy or no mention was made of it. Including their two patients there were 150 in all. Of these, 141 included definite biopsy, a figure it would probably be safer to accept.

Owing to the chronologic proximity of the publication several reports were omitted. Two reports of Young and Davis were included but not the one of January, 1939,[19] in which the former described a new radical operation for carcinoma of the bulbous urethra. In this paper, he stated that the disease had been encountered five times at the Brady Institute. This would add three new cases to the total.

Millin's[14] report of 1932 was not included nor the two cases of Rinker[16] in 1938. Barron's[3] patient is apparently the one operated

upon by Young. The report of Wishard[18] appeared so recently before Kreutzmann's that it is not listed, together with the one patient of the author and those of Davidson and Hankey. For the same reason, presumably, Baillie's[1] paper is not reported. Meland's[12] case is listed but not the one reported in the discussion by Creevy nor the three cases of Cabot, mentioned in the body of the article. In the 1940 *Year Book of Urology* two additional instances are cited from Rothe.[17] In the same year original reports came from Mershon,[13] Barbosa[2] and Grimaldi.[7] Dodson[4] reported one case (1940) and two more in a personal communication to the author which the former will later publish. Riley,[15] in 1941, added an additional case.

If we adopt Kreutzmann's total (148 plus two of his own) of October, 1939, and add to it the twenty-five others mentioned above (including the one following in this report and that of Graves[6]), we have a total of 175 (166 with biopsy). Inasmuch as twenty-four of these twenty-five have come to light in the last three years it would seem pertinent to raise the issue as to the extreme rarity of the disease.*

Kreutzmann's paper is so complete as to bibliography, clinical and pathologic findings and treatment that any additional word would be superfluous since no new facts have appeared. Owing to another author's statement that the disease is especially rare in young individuals it is well to note in passing that in Kreutzmann's tabulation forty patients (27 per cent) were fifty years of age or less. Referring again to Kreutzmann's table, history of gonorrhea was noted in sixty patients, not mentioned in fifty-three, and definitely denied in twenty-nine. This leaves us with a large number of explanations if we wish to adopt gonorrhea and stricture as potent

*It is only fair to state that this opinion is speculative. Dr. R. C. Graves[6] reports that of the 19,000 admissions to the Pondville State Hospital (Mass.) suffering from cancer in the last fourteen years, there have been fifty-five cases of carcinoma of the penis and one of the male urethra. A personal communication from Dr. R. T. Gilchrist[5] of the Northwestern Mutual Life Insurance Company of Milwaukee, states that in a group of 22,063 death claims there were no instances of primary carcinoma of the male urethra, although there were four by extension from elsewhere.

A personal communication from Dr. Charles L. Christiernin of the Metropolitan Life Insurance Company on June 27, 1941, states that their statistical division has examined the causes of death among 555,122 weekly premium paying industrial death claims occurring during the years 1936 to 1939, inclusive, and among 71,976 ordinary department claims for the same period. The cause of death under twenty-three of the industrial and two of the ordinary claims was listed as cancer of the urethra. Corresponding annual death rates from cancer of the urethra were 0.3 and 0.2 per million respectively. It appears from these data that carcinoma of the urethra is an infrequent cause of death. Dr. Christiernin further states that all tabulations by cause of death are necessarily dependent on the reliability of the diagnoses, but that it is felt that they are substantially correct. Of the above twenty-three industrial claims six were males and seventeen females. The corresponding annual death rates for cancer of the urethra were 0.2 and 0.4 million respectively. Both of the ordinary claims were reported as males.

etiologic factors. In these patients who do have stricture, one cardinal classical diagnostic feature is sure to be impressive—namely, the development of sudden, marked increased difficulty in the dilation of strictures which have been previously instrumented for some time. This finding is repeatedly mentioned by many authors. It might be well if we would routinely use the urethroscope on patients suffering from strictures of long standing which have undergone multiple instrumentation, removing a piece of tissue for biopsy in suspicious casees.

Our own patient,[18] operated upon in 1936, was alive and well with no evidence of recurrence in 1939. This is in accord with the findings of others, to wit: that the prognosis is better when the lesion is in the penile urethra. Our patient graciously offered us the possession of his body for examination upon death; but, like the lady of our state who was the first to have a gall-bladder operation, he has been lost from view so that this was or will be impossible. We wish to report at this time an additional example of carcinoma of the male urethra, illustrating less radical treatment (electrocoagulation, radium and x-ray) with satisfactory results to date (May 31, 1941).

A white, married, American man, aged sixty, restaurant proprietor, was referred to us (H.O.M.) by Dr. H. S. Leonard on January 17, 1933, complaining of painless hematuria and sanguinous ejaculation of twenty-four days' duration. He had no other complaints. He voided with normal vigor and volume. The family and past history were irrelevant save for abnormal parental longevity and gonorrhea at the age of twenty-five. There were no children.

The urine was not abnormal when first seen. The patient was not examined but was sent to the hospital for complete study on January 18, 1933. At this time general physical examination gave no positive findings relevant to the present illness. The genitals were normal. Rectal examination revealed a benign hypertrophy of the prostate, size I. Laboratory data (including urinalysis, function test, Kline, original roentgenogram, blood count and coagulation test) were within normal limits. Cysto-urethroscopic examination on January 18, 1933, revealed a normal bladder with contraction and elevation of its outlet without trabeculation. The supraclive was not remarkable. The verumontanum was red and edematous. In the membranous urethra there was a small papilloma which was coagulated. Silver nitrate was applied from time to time to the veru. The patient was dismissed later in the day, and had chills and fever at home that night. During regular intervals until July 10, 1933, the patient came to the office ten times for topical application of silver nitrate to the veru. He then moved to Akron and

was referred to Dr. H. L. Sanford of Cleveland. His acquaintance was renewed on May 11, 1939, when he returned complaining of sifter-spout stream of feeble force, swelling of the glans penis and sanguinous nocturnal emissions, a progressive train of symptoms for about one year. From the later part of 1933 to 1938 he was entirely free of symptoms.

Physical examination in May, 1939, gave positive findings of one palpable left inguinal gland (no record in 1933). The prostate was very slightly enlarged (benign). The glans penis was swollen, firm and edematous. The penis was normal proximal to this area. Protruding from the meatus was a very small, free, proliferative mass less than 1 mm. in diameter. The urine contained a moderate number of pus cells. Dark field and Kline test were negative. There was no external growth nor ulcer. Having recently observed a primary carcinoma of the urethra, we at once applied a similar diagnosis to the present patient.

On May 19, 1939, endoscopic examination was performed with cocaine anesthesia. Dilation tantamount to divulsion was required with a 24F sound to introduce a urethroscope, the veru and floor of the prostatic urethra had a slightly granular appearance. There was bleeding and no evidence of proliferative tissue. On the right side of the distal 2 cms. of the urethra there was a kidney-colored, bleeding, proliferative lesion which seemed to be invading the urethra throughout the site of origin. The urethroscope was removed and a piece of the suspected tissue removed blindly by the use of the Lowsley biopsy rongeur without the sheath. Dr. H. M. Banks gave the following report:

"Histologic examination shows neoplastic structure composed of cells in bulbous-like masses forming tiny lobules clustered together by stroma-supporting cells derived from transitional epithelium, the outer surface of which presents well differentiated cells. Toward the center of the clusters one finds undifferentiated almost embryonic cells resembling embryonic type of transional epithelium. The cells are arranged in bizarre patterns with wild arrangement of nuclear structure and abundant atypical mitoses. Transitional type carcinoma, Grade IV."

At Dr. Banks' suggestion the bladder was again inspected but no abnormality found other than early benign prostatic hypertrophy.

On June 5, 1939, the entire right side of the distal 2 cms. of the urethra was deeply electrocoagulated. Catheterization was never necessitated.

The problem was fully explained to the patient, who was told that in all probability he would have to part with his phallus. If we could count on his continued coöperation, however, we suggested consultation with a roentgenologist. It was finally agreed to apply radium. amputation to be reconsidered at any time the lesion might advance.

Drs. R. C. Beeler and J. N. Collins gave a total of 380 milligram hours in five treatments from June 19 to June 28, 1939. The lesion

was treated directly with radium in a capsule 1 mm. of silver thickness. During this treatment the patient was continually on the verge of a retention which never quite materialized. In addition, thirty treatments of x-ray irradiation were given over the pelvis and perineum as follows—left anterior pelvis, 1,581 r units; right anterior pelvis 1,548 r units; left posterior pelvis 1,926 r units; right posterior pelvis 2,090 r units; right lateral pelvis 736 r units; left lateral pelvis 736 r units; perineum direct, 586 r units; glans penis 1,601 r units.

Response was prompt, the swelling and induration showing regression by the time radium therapy was finished. The patient was seen at frequent intervals, the swelling and edema being less at each successive visit.

By August 29, 1939, all swelling and edema had subsided with the exception of a slight edema of the frenum which has persisted to date. By October 4, 1939, the glans regressed to normal size and has remained so. The inguinal glands decreased in size and are now small, shotty glands which the patient says are the same as they have been for years.

Dense fibrosis of the terminal 2 cms. of the urethra has required regular dilation ever since the swelling and edema disappeared. A meatotomy was performed preliminary to urethroscopy on October 17, 1939, and the urethra dilated to 24F. At that date examination of the urethra showed no evidence of the original tumor tissue and a fresh fissure on the floor of the fossa navicularis due to overdilation. The pendulous urethra was abnormally pale and lacking in its customary elasticity and moisture. On withdrawal of the urethroscope the lumen of the pendulous urethra had a tendency to remain open rather than to collapse around the end of the withdrawing instrument. This peculiarity has persisted. The corpora cavernosa had a dead, leathery consistency, smooth, not nodular nor indurated. This also obtains at the time of writing.

Between October 17, 1939, and April 4, 1941, urethroscopy and dilation of the anterior urethra have been performed seven times. On April 4, 1941, no recurrence was observed, as has been the case at preceding examinations since the first one following completion of irradiation. Quarterly examinations are contemplated for the indefinite future. Urinalysis has been normal.

Symptomatically the patient has felt well and has retained his normal nutrition. He voids freely, though by the end of a quarter he feels the need of dilation. He experiences no pain, has no hematuria and is devoid of libido. The prostate per rectum is unchanged. Minimal evidence of generalized arteriosclerosis has developed. In June, 1940, after physical indiscretion, he had for several weeks mild cardiac insufficiency, which, according to his internist, Dr. S. S. Caplin, was on a sclerotic basis and disappeared without recurrence under restraint and digitalis. Complete physical examination at the time of the last urethroscopy showed no suggestion of remote metastasis.

We present this report, not as an example for therapy, but as an instance of a one-time rare, but progressively less so, cancer of the male urethra, illustrating a favorable result to date, and treated by conservatism which could, at the sign of recurrence, have been altered to more radical methods. With an unintelligent, uncooperative patient we would not have felt at liberty to adopt such a conservative course, without extensive experience to demonstrate its advisability.

SUMMARY

An attempt is made to bring the bibliography of primary carcinoma of the male urethra up to date through May 31, 1941. We have endeavored to mention by title at least, those reported since Kreutzmann's[10] paper in 1939. Any omissions are entirely unintentional. The total number of instances would seem to be 166 substantiated by biopsy. The case of Legueu[11] is not included because we have been unable to obtain the report and do not know if a biopsy was made. For a complete survey of the bibliography (through 1939), signs, symptoms, prognosis, diagnosis and treatment, the reader is referred to the definitive paper of Kreutzmann.[10] We have included an additional instance of carcinoma of the male urethra treated by radium, x-ray and electrocoagulation with apparent success for two years at least without evidence of recurrence, but no claim is made for originality of method.

BIBLIOGRAPHY

1. Baillie, M. H.: Primary carcinoma of male urethra. British Jour. Urol., 11:251-255, 1939.
2. Barbosa de Barros, J.: Primary carcinoma of the male urethra: Case. Rev. Assoc. paulista de med., 17:13-23, (July) 1940.
3. Barron, W. R.: Squamous cell epithelioma of the male urethra: Case. Urol. and Cut. Rev., 44:637-638, (Oct.) 1940.
4. Dodson, A. I.: Transplants from the scrotum for urethral defects. Trans. Amer. Assn. G.-U. Surg., 33:211-220, 1940; *also* personal communication, 1941.
5. Gilchrist, R. T.: Personal communication from Medical Department of Mutual Life Insurance Co. of Milwaukee, (June 18) 1941.
6. Graves, R. C.: Personal communication of data in process of publication, 1941.
7. Grimaldi, F. E., and Mackintosh, M.: Primary epithelioma of perineal urethra: Case. Rev. argent. de urol., 9:267-274. (May-June) 1940.
8. Hutchinson, J.: Epithelial cancer of the mucous membrane of the urethra. Trans. Path. Soc. London, 13:167-169, (Feb. 18) 1862.
9. Kirwin, T. J.: Primary epithelioma of the urethra. Jour. Urol., 27:536-560, (May) 1932.

10. KREUTZMANN, H. A. R., and COLLOFF, B.: Primary carcinoma of the male urethra. Arch. Surg., 39:513-529, (Oct.) 1939; also Jour. A.M.A., 110: 184, (Jan. 15) 1938.
11. LEGUEU: Cancer of the urethra. Med. Mod., 15:313, 1904.
12. MELAND, E. L.: Primary carcinoma of the male urethra. Journal-Lancet, 58:29-32, 1938. (Includes discussion of Creevy.)
13. MERSHON, H. F.: Miss. Valley Med. Jour., 62:40-42, (May) 1940.
14. MILLIN, T.: Carcinoma of the urethra, beginning in the fossa navicularis. Proc. Royal Soc. Med., 26:1221-1222, 1932.
15. RILEY, A.: Epidermoid carcinoma of the perineal urethra. Urol. and Cut. Rev., 45:20-22, (Jan.) 1941.
16. RINKER, J. R.: Primary carcinoma of the urethra in the male: Report of two cases. Urol. and Cut. Rev., 42:874-877, 1938.
17. ROTHE, G.: Primary carcinoma of the urethra in the male: Two cases. Zentralbl. f. Chir., 66:1500-1505, (July 8) 1939.
18. WISHARD, W. N., JR., and BODNER, H.: Primary carcinoma of the male urethra. Jour. Urol., 42:35-46, (July) 1939.
19. YOUNG, H. H.: A new radical operation for carcinoma of the bulbous urethra. Surg., Gynecol., and Obst., 68:77-86, (Jan.) 1939.

DISCUSSION

DR. FLETCHER H. COLBY (Boston, Mass.): I do not feel qualified to discuss the "imponderables," but I would just like to say a word about the x-ray treatment of bladder tumors. At the Huntington Hospitals, we have worked for about four years with the supervoltage unit. We have tried to be not over-enthusiastic about the treatment of bladder tumors with supervoltage radiation and have carefully guarded against any impression that might be given that this might be a curative procedure with bladder tumors.

Our communications in the past have shown that in approximately 50 per cent of the patients who have been treated adequately with supervoltage treatment, the tumors have definitely regressed, that is, the tumor would be reduced to approximately one-third to one-half of its original size. That is what we have termed regression. In about 33 per cent of the patients, the tumors have at one time or another actually completely disappeared, as far as you could tell by cystoscopic examination. This was not regarded as curative by any means.

At the present time, we have approximately seventy patients who have been adequately treated and who have been carefully followed, and again, these statistics are about as I have said; about 50 per cent of the patients have well marked regression of their tumors, and about one-third of the patients have had actual disappearance of the tumors. In many instances, the tumors have eventually recurred. In only a few of the patients have the tumors remained absent from the bladder for long enough periods of time to give you any hope that you might possibly cure certain tumors by external radiation. I think that is very doubtful. On the other hand, you cannot help but have the impression that if you could add a little bit more to external radiation, you might cure some of these tumors, and that is what we have been trying to do during the past year.

We have modified our technique to this extent, that patients are given their preliminary course of external radiation, which is usually 8400 r units. If at the end of three weeks there has been very noticeable, well marked regression of the tumors, then interstitial radiation with gold seeds is added to this, before the tumor has had

a chance to get the effect of the external radiation. Then, if the situation warrants it again, the patients are given another 2800 or 3600 r units of external radiation.

There is one point I would like to emphasize that may be one of the imponderables. We have learned that these tumors will regress in entirely different ways. That is, we have expected regression to take place in four or five weeks. That is not true of all tumors by any means, and is well illustrated by one patient who just about a year ago was given his preliminary course of external radiation for an epidermoid carcinoma that was about 3 cm. in diameter, on the floor of the bladder. The tumor did not regress under radiation after the first course, and the patient was given the second course, which amounted to a total of 12,000 r units; a good preliminary course of radiation. Again, there was no evidence of the tumor regressing.

The patient was forty-eight years of age, in good general condition, without any changes in the upper urinary tract, and seemed to me suitable for total cystectomy, so his right ureter was transplanted to his sigmoid without event.

His left ureter was transplanted, and the patient died in about ten days of a blood stream infection. He was autopsied, and his tumor by this time had regressed to an area that was only about a centimeter in diameter, and the histologic sections show only small nests of active tumor cells, with a great deal of fibrosis. In other words, the patient, in the meantime, had had such marked regression that we were not justified in attempting any such radical procedure as total cystectomy, and if some interstitial radiation perhaps had been added to this patient, he certainly would have had a much better chance.

Dr. George G. Smith (Brookline, Mass.): I should like to ask two questions. I should like to ask Dr. Barringer if he has seen any effects on micturition from the use of alcohol injections.

I should like to ask Dr. Nesbit what is probably a very ignorant question, but is there any difference between eserine and prostigmine, and, if not, why isn't eserine a much cheaper drug to use?

Dr. David M. Davis (Philadelphia, Pa.): I should like to follow Dr. Smith in raising the question of the best means of doing away with pain. I have conferred about this matter with Dr. Fran-

cis Grant in Philadelphia, who favors chordotomy, rather than alcohol injection. I have personally been called upon to see two patients with complete paraplegia and incontinence of urine and feces following alcohol injection. That really makes them worse off than before.

Dr. Austin I. Dodson (Richmond, Va.): I should like to say just a word about Dr. Wishard's paper. Within the last three years —having never seen a case before—I have had three cases of carcinoma of the urethra. The first of these was an elderly man whose urethra had been divided and transplanted into the scrotum, because of a stricture following gonococcal infection.

This man came in almost moribund, an external ureterostomy was done for drainage, with the hope of doing something for the tumor later. He died rather quickly. The autopsy showed squamous cell carcinoma involving the urethra and scrotum.

The second patient was reported last year in my paper on the use of the scrotum for reconstruction of defects in the perineum and urethra. He had no history of gonorrhea or previous stricture. He consulted a urologist who did a resection of his prostate from which he believed the bleeding to be coming. Later, the man developed a peri-urethral abscess. A resection of the perineal portion of his urethra, including the penis, was done and a repair made by turning down a flap of the urethra posteriorly and using the subcutaneous structure of the scrotum to fill in and cover over in front.

The third case had a history of a stricture which had been treated following an attack of gonorrhea and came with a peri-urethral abscess. This patient I treated according to the method, described recently by Dr. Young, of resection and re-anastomoses of the corpora and urethra. These two patients are appearing about once a month for dilatation of the urethra. They both have perfectly smooth perineal wounds with no evidence of any recurrence, one almost three years and one about one year following operation. In neither case was there any palpable gland, except in one where there was one small node which was removed for examination and found to be inflammatory. An outstanding feature in these three cases was an abscess at the cite of the cancer which was similar to the type of perineal abscess that is found in cases of advanced stricture of the urethra. I don't know how many I've missed

in past years where biopsy material was not taken from cases of this type.

DR. BENJAMIN S. BARRINGER (New York, N. Y.): Before going into the matter of alcohol injections, we made a reasonably thorough survey of the different possibilities. Dr. Hyslop, our neurologist, at the Memorial Hospital, was very much against it. He said he had seen cases of both bladder and rectal incontinence following it, and he was thumbs down on it.

Then I asked Dr. B. P. Stookey, neurological surgeon at the Presbyterian Hospital, to come down and talk to us about sympathectomy and chordotomy. He did. This is a major operation with perhaps 15 per cent mortality. It does not succeed in all cases, by any means. If I remember rightly, it succeeds in controlling the pain in only some 40 per cent of cases.

Because of these two factors, I believe that we were justified in trying the alcohol intraspinous injections after the method advocated by Dr. Stern of New York City. I used it, and I still use it, only in patients that I believe are dying of carcinoma and that have intractable pain. We have never gotten rectal or bladder incontinence, with patients that have lived long enough. They were hopelessly sick of the carcinoma. I presume I shall get incontinence, but if I stick to the dictum never to give injections to patients except to those that I believe are hopelessly ill of the disease, I think it will be pretty safe. I'd rather give them incontinence if I can control their pain for the few months that they may live.

Queerly enough, three of these patients that I gave it to were not apparently hopelessly ill. I have given it, I think, in fifteen cases in all, to date, and over a period of a little more than two years, so you see we don't give it very freely and easily.

DR. GEORGE R. LIVERMORE (Memphis, Tenn.): Tell us the method, the technique.

DR. BARRINGER: The method is very simple. We have kept it to the one technique. The patient is put on his side in bed, with the buttocks higher than the head so that the alcohol injection will run toward the lower spine, rather than otherwise. He is placed on the side (if you can determine it) on which the pain is least. If it is on the right side, he is placed on his left side, curled up in bed.

Then, with the smallest spine needle that I dare use, between

the last dorsal and the first lumbar space (I am quite sure I have gone between the first and second lumbar, occasionally, but if I can't do the one, I do the other), I place the needle in the space and very slowly, taking two minutes, inject the quantity of alcohol that is wanted. It comes in ampules which are specially sterilized. I originally started with eight minims, which was being used at that time. At the present time I use twelve minims the first injection. If that doesn't succeed, then four days later I turn him on the other side and again do a similar procedure, giving him perhaps fourteen minims. I have never gone about fourteen minims.

One really ought to have a carpenter's level, to see about the level, but the buttocks should be higher than the head. The patient is left in that position with the buttocks higher than the head for about four hours. It is a little uncomfortable, but a person can stay in that position pretty well.

I think it is a very extraordinary method of dealing with pain. It is the most satisfactory method I have ever seen in dealing with pain in the totally intractable cases.

Dr. Reed M. Nesbit (Ann Arbor, Mich.): In answer to Dr. Smith's question about eserine and prostigmine, eserin is physostigmine, of course, and according to the most recent text of pharmacology is supposed to have results in action such as nausea and some vascular disturbances which are not supposed to be present in prostigmine. We have not as yet used eserine. We are going to start using it. It is very cheap. Perhaps a year or two from now I can report to you on the use of physostigmine.